SORBIC ACID

(CAS #110-44-1)

GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

ToxServices LLC

Assessment Date: February 22, 2024

Expiration Date: February 22, 2029

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 Sorbic Acid (CAS #110-44-1)

Sorbic acid is a straight chain unsaturated fatty acid. The carboxyl (COOH) group in sorbic acid is very reactive and can form salts with calcium, sodium, and potassium. It functions as a preservative in the food, tobacco, cosmetics, and pharmaceuticals industries, as a flavoring agent and fungistatic agent in foods, as an inhibitor of mold and yeast fermentation in wines, and as a fragrance in cosmetics. Sorbic acid is a non-flammable, non-volatile, white crystalline solid that is soluble in water.

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

- Benchmark 3b
    - Moderate Ecotoxicity (acute aquatic toxicity (AA) and chronic aquatic toxicity (CA))
- Benchmark 3c
    - High Group II Human Toxicity (eye irritation (IrE))

A data gap (DG) exists for endocrine activity (E). As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), sorbic acid meets requirements for a GreenScreen Benchmark™ Score of 3 despite the hazard data gap. In a worst-case scenario, if sorbic acid were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

The original GreenScreen® assessment was performed in 2015 under version 1.2 criteria and ToxServices assigned a Benchmark 3 (BM-3) score. The BM-3 score was maintained with a version 1.4 update in 2024; however, there was a reclassification of a number of endpoints following a weight of evidence evaluation of this chemical's dataset (Appendix H).

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

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

Type I (input data) uncertainties in sorbic acid's NAMs dataset include sorbic acid's NAMs dataset include no or insufficient experimental data for carcinogenicity, endocrine activity, and respiratory sensitization, and lack of established test methods for respiratory sensitization. Sorbic acid's Type II (extrapolation output) uncertainties include lack of defined applicability domains OECD QSAR Toolbox in examination of structural alerts, limitation of *in vitro* genotoxicity assays in mimicking *in vivo* metabolism and their focusing on one or only a few types of genotoxicity events, uncertain *in vivo* relevance of *in vitro* receptor binding activity assays, and the limitations in the examination of structural alerts for respiratory sensitization evaluation that does not account for non-immunologic mechanisms of respiratory sensitization. Some of sorbic acid'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 Sorbic Acid

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

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

GreenScreen® Chemical Assessment for Sorbic Acid (CAS #110-44-1)

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

GreenScreen® Assessment (v.1.2) Prepared By:
Name: Mouna Zachary, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: April 6, 2015

Quality Control Performed By:
Name: Bingxuan Wang, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: April 8, 2015

GreenScreen® Assessment (v.1.4) Updated By:
Name: Deb Remeikas, M.A.
Title: Toxicologist
Organization: ToxServices LLC
Date: January 19, 2024

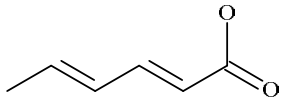
Quality Control Performed By:
Name: Jennifer Rutkiewicz, Ph.D.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: February 22, 2024

Expiration Date: February 22, 2029[2]

Chemical Name: Sorbic Acid

CAS Number: 110-44-1

Chemical Structure(s):



Also called: (2E,4E)-Hexa-2,4-dienoic acid; 2,4-Hexadienoic acid; 2E,4E-Hexadienoic acid; Hexadienoic acid; 2-Propenylacrylic acid (PubChem 2024).

Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):
A relatively complete toxicological dataset was identified for sorbic acid.

Identify Applications/Functional Uses (HSDB 2016, PubChem 2024, EC 2024)**:**
1. Preservative in tobacco, cosmetics, silk-screen inks, noncarbonated beverages, and syrups,
2. Flavoring agent in foods,
3. Fungistatic agent in foods,
4. Inhibitor of mold and yeast fermentation in wines,
5. Fragrance in cosmetics.

Known Impurities[3]:

[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).
[3] Impurities of the chemical will be assessed at the product level instead of in this GreenScreen®.

Heavy metals including lead, mercury, and arsenic are the principle impurities of sorbic acid; however, EFSA 2019 concluded that at the maximum limits as set by the European Commission (EC), sorbic acid, as a food additive, is not a significant source of exposure to these impurities (EFSA 2015, 2019). The current screen is performed on the theoretical pure substance.

GreenScreen® Summary Rating for Sorbic Acid[4,5 6,7]: Sorbic acid was assigned a **GreenScreen Benchmark™ Score of 3** ("Use but Still Opportunity for Improvement") (CPA 2018b). This score is based on the following hazard score combinations:

- Benchmark 3b
  - Moderate Ecotoxicity (acute aquatic toxicity (AA) and chronic aquatic toxicity (CA))
- Benchmark 3c
  - High Group II Human Toxicity (eye irritation (IrE))

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

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

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

Environmental Transformation Products

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

Introduction

Sorbic acid, also known as hexa-2,4-dienoic acid, is a 6-carbon carboxylic acid with two double bonds at C2 and C4 belonging to the class of medium-chain fatty acids (Djoumbo et al. 2016, PubChem 2024).

[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.

Sorbic acid is produced by the catalytic air oxidation of the hexadienal product resulting from the trimerization of acetaldehyde (HSDB 2016, PubChem 2024).

ToxServices assessed sorbic acid 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 2023). It can be accessed at: http://www2.epa.gov/saferchoice/safer-ingredients. Chemicals on the SCIL have been assessed for compliance with the Safer Choice Standard and Criteria for Safer Chemical Ingredients (U.S. EPA 2015).

Sorbic acid is listed on the SCIL as a full green circle.

GreenScreen® List Translator Screening Results

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen Benchmark™ 1 chemicals (CPA 2018b). Pharos (Pharos 2024) is an online list-searching tool that is used to screen chemicals against all of the lists in the List Translator electronically. ToxServices also checks the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b),[8] which are not considered GreenScreen® Specified Lists but are additional information sources, in conjunction with the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for sorbic acid can be found in Appendix C.

- Sorbic acid is an LT-UNK chemical and BM-2 (expired) when screened using Pharos, and therefore a full GreenScreen® is required.
- Sorbic acid is not listed on the U.S. DOT list.
- Sorbic acid is on the following list for multiple endpoints. Specified lists for single endpoints are reported in individual hazard endpoints in the hazard assessment section below.
    - German FEA - Substances Hazardous to Waters - Class 1 - Low Hazard to Waters.

Hazard Statement and Occupational Control

No Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statements were identified for sorbic acid; however, it was classified by the authors of the REACH dossier and the majority of notifiers in the C&L inventory, as indicated in Table 1. Recommended personal protective equipment (PPE) and identified occupational exposure limits (OEL), if any, are summarized in Table 2.

Table 1: GHS H Statements for Sorbic Acid (CAS #110-44-1) (ECHA 2024a,b)

H Statement	H Statement Details
H315	Causes skin irritation.
H319	Causes serious eye irritation

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

Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for Sorbic Acid (CAS #110-44-1)			
Personal Protective Equipment (PPE)	**Reference**	**Occupational Exposure Limits (OEL)**	**Reference**
Safety glasses, protective gloves, and clothing, use local exhaust or breathing protection	ILO 1998	None identified	ILO 1998

Physicochemical Properties of Sorbic Acid

Sorbic acid is a white crystalline solid that is soluble in water. It has a very low vapor pressure, indicating it is unlikely to volatilize, and its log K_{ow} indicates that it has a low potential for bioaccumulation.

Table 3: Physical and Chemical Properties of Sorbic Acid (CAS #110-44-1)		
Property	**Value**	**Reference**
Molecular formula	C6H8O2	PubChem 2024
SMILES Notation	CC=CC=CC(=O)O	PubChem 2024
Molecular weight	112.13 g/mol	PubChem 2024
Physical state	Solid	ECHA 2024a
Appearance	White, crystalline	ECHA 2024a
Melting point	120-150°C (OECD Guideline 102)	ECHA 2024a
Boiling point	Decomposition at 160-260°C (OECD Guideline 103)	ECHA 2024a
Vapor pressure	1.8×10^{-4} Pa (1.4×10^{-6} mm Hg) at 20°C (OECD Guideline 104)	ECHA 2024a
Water solubility	1,560 mg/L at 20°C (OECD Guideline 105)	ECHA 2024a
Dissociation constant	pKa = 4.48-4.69 at 20°C (OECD Guideline 112)	ECHA 2024a
Density/specific gravity	1.2 g/cm3 at 20°C (OECD Guideline 109)	ECHA 2024a
Partition coefficient	Log Kow = 1.32 (at pH = 2.5) and -1.72 (at pH = 6.5) at 20°C (OECD Guideline 117)	ECHA 2024a

Toxicokinetics

- *Absorption*: No direct data were identified for absorption via dermal and inhalation routes of exposure.
    - *Oral:* Sufficient evidence in toxicokinetic studies in mice, rats, and rabbits to single oral doses of sorbic acid found that it was rapidly and almost entirely absorbed in the gastrointestinal tract (CIR 1998, ECHA 2024a).
- *Distribution:* Sorbic acid is rapidly and widely distributed throughout the body.
    - *Oral:* In a toxicokinetic study with rats exposed to a single oral dose of 920 mg/kg radioactive sorbic acid, it was found in internal organs and blood (3%), skeletal muscles (3%), and other parts of the body (6.6%) including lipid deposits and skin, but not in the liver (CIR 1998, EFSA 2015).
- *Metabolism:* Identical in both animals and humans, sorbic acid is almost completely metabolized to carbon dioxide and water via a metabolic pathway similar to common fatty acids, which includes

activation by coenzyme A, hydration by crotonase to a beta-hydroxy acid, dehydration to a beta-keto acid, and cleavage by a beta-keto-thiolase. Sorbic acid metabolism lacks the first reaction step of beta-oxidation because sorbic acid already has an alpha-beta bond (EFSA 2015, ECHA 2024a). Additionally, remaining traces of sorbic acid may be converted via oxidation to trans, trans-muconic acid (CAS# 3588-17-8), also known as muconic acid (EFSA 2015, PubChem 2024).

- *Excretion:* Toxicokinetic studies in animals found that elimination as carbon dioxide via expiration rapidly takes place with a half-life in the range of 40 to 110 minutes, depending on the initial dosage received.
    - *Oral:* Both the mouse and rat studies found that 85% of the total amount of sorbic acid was oxidized within a few hours. In rabbits 4% of sorbic acid and muconic acid were found in the urine within 4 days (EFSA 2015, ECHA 2024a).

Summary: Overall, limited data were available on the toxicokinetics of sorbic acid via the dermal and inhalation routes; however, sufficient evidence in animals exposed to oral doses of sorbic acid found rapid and complete absorption in the gastrointestinal tract. Sorbic acid is distributed rapidly and widely throughout the body, and metabolized ultimately to carbon dioxide and water with up to 85% excreted via expiration. Sorbic and muconic acids (up to 4%) are also excreted in the urine (CIR 1998, EFSA 2015, ECHA 2024a).

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

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

Sorbic acid was assigned a score of Low for carcinogenicity based on negative results in long-term cancer studies in mice and rats. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on reliable data for the target chemical.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2024a
    - In a non-GLP compliant chronic toxicity and carcinogenicity study, ASH/CS1 mice (48 male/dose; 50female/dose) were provided feed containing 0, 1, 5, or 10% sorbic acid (purity ≥ 99%) for 80 weeks. The animals were evaluated for clinical signs of toxicity, body weight, hematology, gross pathology, and histopathology. No evidence of any treatment-related tumors was reported under the test conditions and study authors concluded that dietary levels up to 10% of sorbic acid for 80 weeks caused no carcinogenic effects in mice (Klimisch 2, reliable with restrictions).
    - In another non-GLP compliant chronic toxicity and carcinogenicity study, Wistar rats (48/sex/dose) were provided feed containing 0, 1.5, and 10% sorbic acid (purity > 99%) for 2 years. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, clinical chemistry, urinalysis, gross pathology, and histopathology. No evidence of any treatment-related tumors was reported under the test conditions and study authors concluded that dietary intake of up to 10% sorbic acid for 2-years caused no carcinogenic effects in rats (Klimisch 2, reliable with restrictions).

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

Sorbic acid was assigned a score of Low for mutagenicity/genotoxicity based on negative results in an Ames reverse mutation assay, an *in vivo* micronucleus assay, and an *in vivo* chromosomal aberration assay. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when negative data are available for both gene mutations and chromosome aberrations, and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on reliable data for the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2024a
  - *In vitro*: Sorbic acid (purity not reported, DMSO vehicle) was not mutagenic in a bacterial reverse mutation assay using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100, and *Escherichia coli* strains w3110 and p3478, and *Saccharomyces cerevisiae* strain D4 exposed at up to 500 µg/plate with and without metabolic activation. Cytotoxicity was not specified. The authors did not report control data (Klimisch 2, reliable with restrictions).
  - *In vitro*: Sorbic acid (99% purity, DMSO vehicle) was not genotoxic in an unscheduled DNA synthesis assay using Human cell line A 549 exposed at up to 2,000 µg/mL with and without metabolic activation. Cytotoxicity was noted at the highest concentration. The authors did not report control data (Klimisch 2, reliable with restrictions).
  - *In vivo*: Sorbic acid (99% purity, sesame oil vehicle) was not clastogenic in a GLP-compliant mammalian erythrocyte micronucleus test conducted according to OECD Guideline 474. NMRI mice (5/sex/dose) were administered via gavage a single dose of sorbic acid (purity > 99%) at 0, 500, 1,500, or 5,000 mg/kg. There was no increase in the frequency of micronucleated erythrocytes with treatment. Cytotoxicity was not specified. The authors did not report control data (Klimisch 2, reliable with restrictions).
  - *In vivo*: Sorbic acid (> 99% purity, carboxymethylcellulose vehicle) was not genotoxic in a sister chromatid exchange assay using NMRI mice (6/sex/dose) administered via gavage a single dose of sorbic acid (purity > 99%) at 0, 500, 1,500, or 5,000 mg/kg. There was no increase in the frequency of sister chromatid exchanges with treatment. Clinical signs of toxicity were reported at the top dose. The authors did not report control data (Klimisch 2, reliable with restrictions).
  - *In vivo*: Sorbic acid (99% purity, distilled water vehicle) was not clastogenic in a chromosome aberration test using male Swiss mice (n=10) administered via gavage sorbic acid (purity 99%) at 0 or 15 mg/kg/day for 30 days. There was no increase in the frequency of chromosomal aberrations with treatment. Systemic toxicity was not specified. The authors did not report control data (Klimisch 2, reliable with restrictions).

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

Sorbic acid was assigned a score of Low for reproductive toxicity based on the lack of reproductive effects observed up to 3,000 mg/kg/day in an OECD Guideline 443 one-generation and an OECD Guideline 416 two-generation oral reproduction toxicity study in rats exposed to the target chemical. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on reliable data from a guideline study for the target chemical.

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

    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2024a
    - In a GLP-compliant extended one-generation reproductive toxicity study conducted according to OECD Guideline 443, Crl:CD (SD) rats (25/sex/group) were provided feed containing 0, 15,000, 30,000, or 60,000 ppm sorbic acid (purity 100%) for 2 weeks prior to mating and presumably through gestation and lactation. Selected F1 generation animals then underwent the same treatment process. No changes to estrous cycle, sperm parameters, or reproductive performance were measured with treatment for the P0 generation. In the F2 generation, pup body weight at the high dose was reduced and the authors of the REACH dossier considered this to be an adverse developmental effect. Based on lower food consumption, body weights, and weight gains in all cohorts, the authors of the ECHA dossier assigned a reproductive NOAEL of 30,000 ppm, equivalent to 3,000 mg/kg/day (Klimisch 1, reliable without restrictions).
        - In EFSA's review of this study, they reported effects including decreased ovary and uterus weights in high dose F1 females, decreased body weight gain in mid- and high-dose F0 females during gestation and lactation and in F1A males, decreased food intake in mid- and high-dose F0 and F1 animals, increased plasma cholesterol levels in mid- and high-dose F0 females and high-dose F1A males and females, decreased pup body weight in mid-and high-dose F2 pups and high-dose F1 pups, increased liver weight in high dose F0 and F1A males, and decreased mean and absolute and relative ovary and uterus weights in F1B female. Overall, they considered the decrease in F2 generation pup body weight gain at the high dose to be the most biologically relevant effect and derived a BMDL of 1,110 mg/kg/day, which they used to derive the ADI (EFSA 2019).
    - In a GLP-compliant two-generation toxicity study conducted according to OECD Guideline 416, Crj: CD(SD) rats (parental (F0) (30/sex/group) and first generation (F1) (25/sex/group)) were administered doses of 0, 300, 1,000, or 3,000 mg/kg/day sorbic acid (purity 99.9%) via gavage from 10 weeks before mating until day 21 of lactation. F1 pups were not selected for mating until 7 weeks after birth. The parental animals were evaluated for clinical signs of toxicity, body weight, food consumption, testes and epididymis weights, ovaries weights, estrus cycle, gross pathology, and histopathology. Hematology and blood serum chemistry were only evaluated in parental males. Reproductive parameters (pregnancy rate, length of gestation, implantations, corpora lutea, and resorptions) were also evaluated in parental animals. There were no treatment-related effects on any of the fertility or reproductive indices measured. Based on the lack of treatment-related effects, the authors of the REACH dossier assigned a reproductive toxicity NOAEL of 3,000 mg/kg/day, the highest dose tested (Klimisch 1, reliable without restrictions).

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): L
Sorbic acid was assigned a score of Low for developmental toxicity based on the lack of developmental effects up to 1,000 mg/kg/day in guideline one-generation and two-generation oral reproduction toxicity studies in rats and in a pre-natal developmental toxicity study in rabbits on the target chemical. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on reliable data from a guideline study for the target chemical.

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

- ECHA 2024a
    - In a GLP-compliant extended one-generation reproductive toxicity study conducted according to OECD Guideline 443, Crl:CD (SD) rats (25/sex/group) were provided feed containing 0, 15,000, 30,000, or 60,000 ppm sorbic acid (purity 100%) for 2 weeks prior to mating and presumably through gestation and lactation. Selected F1 generation animals then underwent the same treatment process. No treatment-related developmental effects were reported in the F1 generation. In the F2 generation, pup body weight at the high dose was reduced and the authors of the REACH dossier considered this to be an adverse developmental effect. Based on this they assigned a developmental NOAEL of 30,000 ppm, equivalent to 3,000 mg/kg/day based on their calculations (Klimisch 1, reliable without restrictions).
        - In EFSA's review of this study, they reported effects including decreased ovary and uterus weights in high dose F1 females, decreased body weight gain in mid- and high-dose F0 females during gestation and lactation and in F1A males, decreased food intake in mid-and high-dose F0 and F1 animals, increased plasma cholesterol levels in mid- and high-dose F0 females and high-dose F1A males and females, decreased pup body weight in mid-and high-dose F2 pups and high-dose F1 pups, increased liver weight in high dose F0 and F1A males, and decreased mean and absolute and relative ovary and uterus weights in F1B female. Overall, they considered the decrease in F2 generation pup body weight gain at the high dose to be the most biologically relevant effect and derived a BMDL of 1,110 mg/kg/day, which they used to derive the ADI (EFSA 2019).
    - In a GLP-compliant two-generation toxicity study conducted according to OECD Guideline 416, Crj: CD(SD) rats (parental (F0) (30/sex/group) and first generation (F1) (25/sex/group)) were administered doses of 0, 300, 1,000, or 3,000 mg/kg/day sorbic acid (purity 99.9%) via gavage from 10 weeks before mating until day 21 of lactation. F1 pups were not selected for mating until 7 weeks after birth. The parental animals were evaluated for clinical signs of toxicity, body weight, food consumption, testes and epididymis weights, ovaries weights, estrus cycle, gross pathology, and histopathology. Offspring were evaluated for survival, number and sex of pups, body weight, and external and internal abnormalities. Treatment-related effects on parental animals included reduction in food consumption in high dose males and females of the P and F1 generations during the pre-mating period, and also in high dose females during gestation and lactation periods. The authors attributed this effect to the increased caloric intake resulting from the metabolizable sorbic acid. There was no other compound-related toxicity. Authors noted adverse effects on growth (body weight and weight gain), attainment of developmental landmarks (cleavage of the balanopreputial gland and vaginal opening), and behavioral changes in the F1/F2 offspring of the high dose group during lactation. Based on this, the authors of the REACH dossier assigned a developmental toxicity NOAEL of 1,000 mg/kg/day (Klimisch 1, reliable without restrictions).
    - In a GLP-compliant prenatal developmental toxicity study conducted according to OECD Guideline 414, pregnant female Himalayan rabbits (20/dose) were administered sorbic acid (purity 99.9%) via gavage at doses of 0, 300, 1,000, or 3,000 mg/kg/day from gestation day 6 to 29. The pregnant animals were evaluated for clinical signs of toxicity, body weight, food consumption, ovaries and uterine content, gross pathology, and histopathology. Reproductive parameters (corpora lutea, implantation and resorptions) were also evaluated in the treated animals. Offspring were evaluated for survival, number and sex of pups, body weight, and external and internal abnormalities. Authors noted treatment-related maternal and developmental toxicity at doses greater than 300 mg/kg/day. Maternal effects at 1,000

mg/kg/day included increased respiratory rate, decreased body weight gain, and rough surface of the spleen. Maternal findings in high dose females included increased respiratory rate, mortality (8/20 does, abortion (11 does), decreased body weight and body weight gain, marked decrease in food consumption, and pathological findings upon necropsy (rough surface and reduced size of the spleen). Developmental effects at 3,000 mg/kg/day, which produced severe maternal toxicity, included increased number of resorptions and abortions, decreased number of live fetuses, and a statistically significant increase in malformations (malrotated forepaw). The authors considered these severe effects on the offspring and maternal females to be secondary to maternal gastro-intestinal damage from sorbic acid administration, as it is known to have gastric irritant properties and produced gastric lesions, and speculated that the substance disturbed intestinal microflora resulting in nutrient deficiencies. The authors of the REACH dossier identified a maternal toxicity NOAEL of 300 mg/kg/day and a developmental toxicity NOAEL of 1,000 mg/kg/day (Klimisch 1, reliable without restrictions).

- Based on weight of evidence, a score of Low was assigned. Although developmental effects were seen in offspring of dams exposed to sorbic acid orally, these occurred at very high doses of > 1,000 mg/kg, which is the limit dose under reproductive and developmental toxicity study guidelines. Therefore, sorbic acid does not warrant classification as a developmental toxicant.

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

Sorbic acid was assigned a score of Data Gap for endocrine activity due to lack of sufficient 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 2024
  - Sorbic acid was active in [0/15] estrogen receptor (ER) assays, [1/16] androgen receptor (AR) assays, [0/2] steroidogenesis assays, and [0/9] thyroid receptor assays performed as part of the U.S. EPA's Endocrine Disruptor Screening Program (EDSP) in the 21st Century (Appendix D).
- ECHA 2024a
  - In a GLP-compliant extended one-generation reproductive toxicity study conducted according to OECD Guideline 443, Crl:CD (SD) rats (25/sex/group) were provided diets containing 0, 15,000, 30,000, or 60,000 ppm sorbic acid (purity 100%) for 2 weeks prior to mating and presumably through gestation and lactation. Selected F1 generation animals then underwent the same treatment process. There were no changes to anogenital distance (AGD) measured in the F1 or F2 generations on day 1. There were no effects on nipple retention on day 13 for F1 males, and the authors considered effects on nipple retention in the F2 males (two males in one litter at the low dose and one male at the mid dose) to be unrelated to treatment (no details provided). There were no effects on the day of balanopreputial separation in the F1 generation. Vaginal opening was delayed by 3 days in high dose F1 females, but there were no effects on age of vaginal opening in the low and mid dose females. There was no measured change with treatment T4 levels of the F1 generation, and the authors stated that unspecified differences in TSH were due to natural variation. There were no effects on estrous cycle, sperm measures, or reproductive performance (Klimisch 1, reliable without restrictions).
    - In EFSA's review of this study, they agreed that the variation in thyroid hormone levels were not indicative of an adverse effect, and that there were no effects on nipple retention. They also noted decreased weights of the ovaries and uterus in F1

females at the high dose, and although there were no effects on timing to estrous cycle, vaginal opening in high dose females was delayed by 3 days in cohort 1 and 2 days in cohort 2. The EFSA panel noted the lack of effect on AGD and concluded that the reduction in AGD measured in the previously conducted two-generation toxicity study (detailed below) was not relevant for their risk assessment of sorbic acid (EFSA 2019).

    - In a GLP-compliant two-generation toxicity study conducted according to OECD Guideline 416, Crj: CD(SD) rats (parental (F0) (30/sex/group) and first generation (F1) (25/sex/group)) were administered doses of 0, 300, 1,000, or 3,000 mg/kg/day sorbic acid (purity 99.9%) via gavage from 10 weeks before mating until day 21 of lactation. F1 pups were not selected for mating until 7 weeks after birth. There were marginal but statistically significant delays in cleavage of the balanopreputial gland and vaginal opening in high dose F1 pups selected for mating. In addition, AGD was reduced in F2 pups, but the REACH dossier authors considered this related to slightly reduced body weight during lactation and did not consider it adverse. There were no effects on male fertility parameters, estrous cycle, or reproductive performance (Klimisch 1, reliable without restrictions).
- Based on the weight of evidence, a Data Gap was assigned. Two studies reported effects on vaginal opening in rats at relatively high doses (> 3,000 mg/kg/day), and they reported inconsistent effects on AGD, which EFSA concluded are not relevant. There were no effects on fertility and reproduction. However, although data do not indicate endocrine disruption (i.e., adverse health effects related to endocrine activity), data are insufficient to address the potential for endocrine activity.

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

Sorbic acid was assigned a score of Low for acute toxicity based on oral LD_{50} values greater than 5,000 mg/kg in rats and a dermal LD_{50} value greater than 2,000 mg/kg in rats. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD_{50} values are greater than 2,000 mg/kg (CPA 2018b). The confidence in the score is high as it is based on reliable measured data on the target chemical.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2024a
    - *Oral:* LD_{50} = 10,500 mg/kg in Sherman rats (Klimisch 2, reliable with restrictions).
    - *Oral:* LD_{50} = 12,500 mg/kg in male Wistar rats (Klimisch 2, reliable with restrictions).
    - *Oral:* LD_{50} = 9,600 mg/kg in female Wistar rats (Klimisch 2, reliable with restrictions).
    - *Dermal:* LD_{50} (GLP-compliant; OECD Guideline 402) > 2,000 mg/kg in Sprague-Dawley rats (Klimisch 1, reliable without restriction).

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

Sorbic acid was assigned a score of Low for systemic toxicity (single dose) based on a lack of specific organ toxicity in a standard acute dermal toxicity study in rats exposed to the target chemical at 2,000

mg/kg. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (single dose) when there are no effects reported at acute dermal doses greater than 2,000 mg/kg and no GHS classification are available (CPA 2018b). The confidence in the score is high as it is based on reliable measured data on the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2024a
  - *Dermal:* In a GLP-compliant acute dermal toxicity study conducted according to OECD Guideline 402, Sprague-Dawley rats (5/sex) were administered a single dermal application of 2,000 mg/kg sorbic acid (purity not specified) under semiocclusion for 24 hours and then observed for 15 days. No mortality or clinical signs of toxicity were observed, and no gross pathological findings were noted (Klimisch 1, reliable without restriction).

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

Sorbic acid was assigned a score of Low for systemic toxicity (repeated dose) based on a lack of specific organ toxicity at oral doses greater than 100 mg/kg/day in subchronic and chronic studies using rats, mice, and dogs. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when there are no effects reported at subchronic oral doses greater than 100 mg/kg/day and no GHS classification are available (CPA 2018b). The confidence in the score is high as it is based on data from reliable, high quality studies for the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2024a
  - *Oral:* In the previously described chronic toxicity and carcinogenicity study, ASH/CS1 mice (48 male/dose; 50 female/dose) were provided feed containing 0, 1, 5, or 10% sorbic acid (purity ≥ 99%) for 80-weeks (equivalent to 1,400, 7,000, and 14,000 mg/kg/day as calculated by the authors of the REACH dossier). The animals were evaluated for clinical signs of toxicity, body weight, hematology, gross pathology, and histopathology. No mortalities or treatment-related effects on clinical signs of toxicity, food consumption or hematology parameters were noted. There was a statistically significant decrease in body weight gain at the high dose. Hematology examination showed a statistically significant reduction in the hemoglobin concentration of all treated male mice after 13 weeks of administration, in males at 5% sorbic acid after 26 weeks and a statistically significant decrease of red blood cells count (RBC) for low dose males after 26 weeks. The authors considered these findings incidental as they were not noted in females. Statistically significant increases were noted in the relative organ weights of the brain, liver, kidney, stomach, and small intestine of males on both the 5 and 10% sorbic acid diets. All groups of females treated with sorbic acid had increased relative heart and liver weights, and females of the highest dose group also had increased relative brain weight. The higher values for the relative weights of brain, spleen, stomach, and small intestine were noted in the absence of any significant differences in the absolute weights and with no indication of any histological change. The increased values for relative heart weights in females are anomalous as there were no comparable changes in the males. The increase of relative liver weights is considered to be a reflection of an increase in metabolic demand rather than a toxic effect of sorbic acid. The increased relative kidney weight does not represent any marked toxic effect

of sorbic acid, as the histological examination found significantly fewer incidences of lesions in the kidney in treated mice than in the control. Based on effects on organ weights, the authors of the REACH dossier identified a systemic toxicity NOAEL of 1.0%, which is equivalent to 1,400 mg/kg/day (Klimisch 2, reliable with restrictions).

- *Oral:* In the other previously described non-GLP compliant chronic toxicity and carcinogenicity study, Wistar rats (48/sex/dose) received feed containing 0, 1.5, or 10% sorbic acid (purity > 99%) for 2 years (equivalent to 750 and 5,000 mg/kg/day as calculated by the authors of the REACH dossier). The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, clinical chemistry, urinalysis, gross pathology, and histopathology. No mortalities or treatment-related effects on clinical signs of toxicity, food consumption or clinical chemistry parameters were noted. A statistically significant decrease in body weight gain was measured in high dose males and females at week 39, and at week 101 there was a statistically significant decrease in body weight in high dose females only. High dose females had a statistically significant increase in urine volume at weeks 13 and 52. High dose males had a statistically significant increase in blood urea, which the authors attributed to aging. Hematology examination showed a statistically significant decrease in the total leukocyte count in females at the high dose at week 27 and a statistically significant increase in the total red blood cell count in low dose female group at week 52. The authors considered these findings incidental as they were not noted in males. Absolute and relative thyroid weight was increased in males in the high dose group. Signs of advanced renal changes (unspecified) were seen in these males and therefore, study authors stated that the increases in thyroid weight do not represent an effect of sorbic acid on the thyroid, but rather an indirect effect of renal damage on the parathyroid. Relative liver weights were increased in males and females of the 10% sorbic acid group. In addition, the high dose females had higher weights of the kidneys, small intestine, and gonads. However, there were no histopathological findings in these organs. The microscopic examination of the liver of the high dose females showed an increase in focal fatty change, a statistically significantly decrease in the incidence of bile-duct hyperplasia, and a statistically significantly increase in the incidence of focal necrosis. In the high dose males, a statistically significant decrease in the incidence of extra-medullary hematopoiesis in spleen and a decrease of hemosiderin deposition in spleen were observed. Based on effects on clinical chemistry, hematology, and organ weights, the authors of the REACH dossier identified a systemic toxicity NOAEL of 1.5%, which is equivalent to 750 mg/kg/day (Klimisch 2, reliable with restrictions).
- *Oral:* In a GLP-compliant repeated dose toxicity study conducted according to OECD Guideline 408, Sprague-Dawley rats (20/sex/dose) were provided sorbic acid (purity not specified) in feed at concentrations of 0, 25,000, 50,000, or 100,000 ppm for 90 days. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, clinical chemistry, gross pathology, and histopathology. No mortalities or treatment-related effects on clinical signs of toxicity or body weight were noted. Similarly, there were no treatment-related effects on hematology and clinical chemistry. Histopathological examination revealed no treatment-related effects. The authors of the REACH dossier established a NOAEL of 100,000 ppm for systemic toxicity; which they calculated as equivalent to 6,800 mg/kg/day in males and 7,200 mg/kg/day in females (Klimisch 1, reliable without restriction).
- *Oral:* In a GLP-compliant repeated dose toxicity study conducted according to OECD Guideline 407, Sprague-Dawley rats (5/sex/dose) were provided sorbic acid (purity not specified) in feed at concentrations of 0, 25,000, 50,000, or 100,000 ppm for 28 days. Another two groups of rats (5/sex/dose) were provided sorbic acid at concentrations of 0, or

100,000 ppm for 28 days and were monitored for additional 15 days. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, clinical chemistry, urinalysis, gross pathology, and histopathology. No mortalities or treatment-related effects on clinical signs of toxicity or body weight were noted. Similarly, there were no treatment-related effects on hematology, clinical chemistry, and urinalysis parameters. Histopathological examination revealed no treatment related effects. Based on this, the authors of the REACH dossier established a NOAEL of 100,000 ppm for systemic toxicity, which they calculated as equivalent to 9,200 mg/kg/day in males and 8,600 mg/kg/day in females (Klimisch 1, reliable without restriction).

- *Oral:* In a non-GLP-compliant repeated dose toxicity study, mixed cocker, and terrier dogs (n=3) were provided sorbic acid (purity > 99%) in feed at concentrations of 0 or 40,000 ppm for 88-91 days. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, gross pathology, and histopathology. No treatment-related effects were reported. Based on this, the authors of the REACH dossier established a NOAEL of 40,000 ppm for systemic toxicity (Klimisch 2, reliable with restrictions).
    - Using the provided body weights for male (2.425 kg) and female (1.8 kg) dogs for this study and the subchronic food (dry) consumption rates for beagle dogs (U.S. EPA 1988) (in the absence of data on mixed cocker and terrier dogs), ToxServices calculated a NOAEL of 1,363 mg/kg/day (40,000 mg/kg * 0.083 kg/day / 2.435 kg) for males and a NOAEL of 1,644 mg/kg/day (40,000 mg/kg * 0.074 kg/day / 1.8 kg) for females.

Neurotoxicity (single dose, N-single) (Group II) Score (vH, H, M, or L): *L*
Sorbic acid was assigned a score of Low for neurotoxicity (single dose) based on a lack of neurotoxic effects (clinical observation and gross pathology) in a standard acute dermal toxicity study in rats exposed to the target chemical at 2,000 mg/kg. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (single dose) when there are no neurotoxic effects reported at acute dermal doses greater than 2,000 mg/kg and they are not GHS classified (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 2024a
    - *Dermal:* In a GLP-compliant acute dermal toxicity study conducted according to OECD Guideline 402, Sprague-Dawley rats (5/sex) were administered a single dermal application of 2,000 mg/kg sorbic acid (purity not specified) under semiocclusion for 24 hours and then observed for 15 days. No mortality or clinical signs of neurotoxicity was observed, and no gross pathological findings were noted (Klimisch 1, reliable without restriction).

Neurotoxicity (repeated dose, N-repeated) (Group II*) Score (H, M, or L): L
Sorbic acid was assigned a score of Low for neurotoxicity (repeated dose) based on lack of neurotoxic effects at oral doses greater than 100 mg/kg/day in an OECD Guideline 407 subchronic study in rats. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (repeated dose) when there are no neurotoxic effects reported at subchronic oral doses greater than 100 mg/kg/day and no GHS classification are available (CPA 2018b). The confidence in the score is high as it is based on a high quality, reliable study with neurobehavioral exam on the target chemical.

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

    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2024a
    - *Oral:* In the previously described GLP-compliant repeated dose toxicity study conducted according to OECD Guideline 407, Sprague-Dawley rats (5/sex/dose) were provided sorbic acid (purity not specified) in feed at concentrations of 25,000, 50,000, or 100,000 ppm for 28 days. Another two groups of rats (5/sex/dose) received sorbic acid at concentrations of 0, or 100,000ppm for 28 days and were monitored for additional 15 days. Neurobehavioral examination, which included FOB, sensory evaluation, grip strength and motor activity, was performed on the treated rats. No treatment-related effects on these parameters were reported. Therefore, ToxServices established the NOAEL at 100,000 ppm for neurotoxicity for this study. This is equivalent to 9,200 mg/kg/day in males and 8,600 mg/kg/day in females as calculated by the authors of the REACH dossier (Klimisch 1, reliable without restriction).

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

Sorbic acid was assigned a score of Low for skin sensitization based on negative results in an adjuvant guinea pig maximization test and mostly negative results in reliable predictive human patch testing at concentrations up to 20% sorbic acid. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate and negative data and no GHS classification are available (CPA 2018b). The confidence in the score is low as the test substance was not tested up to 100% and no information was provided regarding whether the selection of the top dose was based on irritancy in the animal study, and because some human studies provided mixed results for sensitive individuals.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:*
        - New Zealand – GHS – Skin sensitization – Category 1.
            - Based on contact sensitization in humans (CCID 2024).
- ECHA 2024a
    - In a guinea pig maximization test, Pirbright-Hartley guinea pigs (10/sex) were induced intradermally with 0.1% sorbic acid (purity not specified) and Freund's Complete Adjuvant (FCA) 3 times per week for 3 weeks followed by 0.1% intracutaneous challenge 2 weeks later and then a 1% topical rechallenge after an additional 2 weeks. Reactions were reported in 4 of the 20 animals after the first challenge and none were reported after the rechallenge (Klimisch 2, reliable with restrictions).
        - ToxServices notes that this study deviates from guideline guinea pig maximization tests because it does not include a topical induction following the intradermal induction, and because the first challenge was conducted with an intradermal administration rather than a topical application. Because current guidelines utilize a topical challenge, ToxServices used the response rate (0%) following topical challenge for the classification of this endpoint.
    - Low incidence of skin sensitization reactions was reported in human studies with sorbic acid. A total of 49 out of 1,537 patients had allergic reactions to medication containing sorbic acid (sensitization index 3.1%). In another study, sensitization to sorbic acid containing medications was also reported in 5 out of 736 eczematous patients (sensitizing index 0.6%). In a multicenter study, 20 patients out of 2,912 showed positive reactions to preservatives including sorbic acid. Positive reactions occurred in 10 out of 1,489 patients exposed to 10% sorbic acid within three of four ointment bases.

- CIR 1988
    - CIR summarized a number of human studies of formulations and dilutions of sorbic acid with mixed results. In a human repeat insult patch test (HRIPT) with 93 and 33 volunteers, there were 0/93 and 1/33 positive reactions reported with induction applications of 10% and 20% sorbic acid, respectively, with an overall sensitization rate of 0.8%. In another HRIPT with 181 and 121 volunteers, there were 0/181 and 1/121 positive reactions reported with induction applications of 10% and 20% sorbic acid, respectively, with an overall sensitization rate of 0.33%. In a third Draize-Shelanski HRIPT, 1% sorbic acid in petroleum did not induce sensitization reactions in 50 volunteers. Other studies were also reported; however, these studies were performed in sensitive populations, or with formulation mixtures; therefore, only the more reliable HRIPTs on sorbic acid were reported. Overall, CIR concluded based on these studies that sorbic acid is not a sensitizer.
- Based on the above data, a score of Low was assigned. For the weight of evidence evaluation, ToxServices weighed the animal data more heavily than the human data. GHS criteria indicate that "human data not generated in controlled experiments [(i.e., human repeat insult patch tests (HRIPT)] with volunteers for the purpose of hazard classification can be used with caution" (UN 2023). Although human studies report some positive responses, some of clinical studies were performed in sensitive populations such as dermatology patients and eczema patients and/or with formulation mixtures including substances other than sorbic acid, leading to uncertainty regarding the cause of the positive reactions reported. Furthermore, in three HRIPTs reported by CIR (1988) very low incidence of sensitization at rates of 0%, 0.33%, and 0.8% were reported with induction applications of 1%, 10%, and 20% sorbic acid, respectively. CIR (1988) concluded that sorbic acid is not a skin sensitizer. Based on the negative results in the GPMT, the mostly negative results up to 20% in reliable predictive human patch testing supported by CIR's conclusion, ToxServices did not classify sorbic acid as a skin sensitizer.

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

Sorbic acid was assigned a score of Low for respiratory sensitization based on a lack of dermal sensitization potential and according to ECHA's guidance on respiratory sensitization evaluation. GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when adequate and negative data and no GHS classification are available (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 2023
    - Sorbic acid does not contain any structural alerts for respiratory sensitization (Appendix E)
- Based on the weight of evidence and guidance from ECHA regarding assessment of respiratory sensitization potential, a score of Low was assigned. The guidance from ECHA states that the mechanisms leading to respiratory sensitization are essentially similar to those leading to skin sensitization (ECHA 2017). ECHA recommended that if a chemical is not a dermal sensitizer based on high quality data, it is unlikely to be a respiratory sensitizer. ECHA also noted that this rationale does not cover respiratory hypersensitivity caused by non-immunological mechanisms, for which human experience is the main evidence of activity (ECHA 2017). As sorbic acid 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 sorbic acid, and as sorbic acid does not contain any

structural alerts for respiratory sensitization (OECD 2023), sorbic acid is not expected to be a respiratory sensitizer.

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

Sorbic acid was assigned a score of Low based on negative results in an OECD Guideline 404 test in rabbits exposed to undiluted sorbic acid. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate and negative data and no GHS classification are available (CPA 2018b). The confidence in the score is high as it is based on reliable, high quality measured data for the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - New Zealand – GHS – Skin irritation – Category 2.
      - Based on severe skin irritation in humans (CCID 2024).
- ECHA 2024a
  - Sorbic acid was not irritating in a GLP-compliant OECD Guideline 404 study. New Zealand White rabbits (n=3) were administered 500 mg undiluted sorbic acid (purity 99%) under semiocclusion for 4 hours. The individual mean 24/48/72-hour erythema and edema scores were zero for all three animals (Klimisch 1, reliable without restriction).
  - In the previously described GLP-compliant acute dermal toxicity study conducted according to OECD Guideline 402, Sprague-Dawley rats (5/sex) were administered a single dermal application of 2,000 mg/kg sorbic acid (purity not specified) under semiocclusion for 24 hours and then observed for 15 days. No skin reactions were observed (Klimisch 1, reliable without restriction).
  - Sorbic acid was moderately irritating in a clinical study when applied at 0.1, 0.5, or 1% to the skin of 15 to 17 volunteers for 20 minutes. This study was poorly reported and included application of other chemicals including corticosteroids, steroids, antihistamines, and non-steroidal anti-inflammatory agents (NSAIDs); therefore, leading to the uncertainty that sorbic acid is the cause of irritation (Klimisch 2, reliable with restrictions).
- CIR 1988
  - A dermal irritation test following the Draize principles was performed with three rabbits (sex and strain not specified) administered dermal applications of 1, 5, or 10% of a formulation of sorbic acid in petrolatum (purity not specified) under semi-occlusive dressing (no details about the exposure period and reaction scores were provided). The skin irritation indices were 0.7, 0.2, and 0.5 (maximum = 8) for the 1, 5, and 10% concentrations, respectively. Based on this, the study authors considered sorbic acid as practically not irritating to rabbit skin.
  - In a 3-week repeated dose dermal toxicity study, sorbic acid was applied to the shaved skin of three rats at a concentration of 5% in a lanolin-petrolatum paste for 6 days/week. The paste was massaged lightly into the skin for 2 minutes, and the area was then washed with water and any excess paste wiped away. No irritation to the skin was reported.
  - In a short term dermal repeated dose toxicity study, signs of skin irritation were observed in New Zealand albino rabbits (3/sex) administered 2 ml/kg of a formulation containing 0.5% sorbic acid (pH not specified) dermally 5 days/week for 4 weeks. These included slight to moderate erythema and edema, slight atonia, and slight desquamation. The skin had a mild intradermal inflammatory response. The effects continued throughout the study.
  - A dermal irritation test was performed with nine rabbits (sex and strain not specified) administered dermal applications of a product containing 0.5% sorbic acid (pH not

specified) under occlusive dressing (no details about the exposure period were provided). Erythema and edema were scored 2 and 24 h after removal of the dressing. The primary irritation index (PII) of the test material was 0.72 out of a maximum possible score of 8.0; the skin irritation potential of the material was minimal.
    - In another dermal irritation study, an eye makeup remover that contained 0.10% sorbic acid (pH not specified) was applied to intact and abraded skin of rabbits for 24 h with occlusive patches. The formulation did not irritate rabbit skin.
- Based on the weight of evidence, a score of Low was assigned. Although human data from one study reported moderate irritation up to 1% sorbic acid, animal data from numerous studies, including an OECD Guideline 404 study, indicate that sorbic acid is not irritating. Additionally, the human study evaluated sorbic acid in combination with other chemicals and is poorly reported; therefore, ToxServices weighed the more reliable animal data more heavily than the human data in the weight of evidence evaluation. Overall, based on negative results in an OECD Guideline 404 study in rabbits, ToxServices did not classify sorbic acid as a skin irritant.

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

Sorbic acid was assigned a score of High for eye irritation/corrosivity based on ToxServices classifying it as a GHS Category 2A eye irritant based on an OECD Guideline 405 study using rabbits. GreenScreen® criteria classify chemicals as a High hazard for eye irritation/corrosivity when they are classified to GHS Category 2A classification (CPA 2018b). The confidence in the score is high as it is based on reliable, high quality measured data on the target chemical.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:*
        - New Zealand – GHS – Eye irritation – Category 2.
            - Based on eye irritation in rabbits (CCID 2024).
- ECHA 2024a
    - Sorbic acid was irritating in a GLP-compliant OECD Guideline 405 study. New Zealand White rabbits (n=3) were instilled with 100 mg undiluted sorbic acid (purity > 99%) into the eye for 24 hours. The individual mean 24/48/72-hour iris scores were 1 for all animals with the effects being fully reversible within 7 days. The individual mean 24/48/72-hour chemosis scores were 1.66, 0.66, and 2.33 with the effects being fully reversible within 7 days. The individual mean 24/48/72-hour conjunctiva scores were 3, 2.66, and 3 with the effects being fully reversible within 14 days. The individual mean 24/48/72-hour cornea opacity scores were 1, 1, and 1.33 with the effects being fully reversible within 7 days (Klimisch 1, reliable without restriction). *The results of this study would classify sorbic acid as GHS Category 2A based on iris scores and corneal opacity scores equal to or greater than 1 in at least 2 of the 3 animals, and conjunctiva scores of greater than 2 in at least 2 of the 3 animals, which are fully reversible within an observation period of 21 days (UN 2023).*
- CIR 1988
    - An ocular irritation test following the Draize principles was performed with rabbits (3/dose; sex and strain not specified) administered ocular instillations of formulations containing 1, 5, or 10% sorbic acid in petrolatum (purity not specified). The animals were evaluated at 1, 2, and 24 hours and daily until all irritation had disappeared. The ocular irritation indices at 24 hours were 0.7, 0.7, and 2 (maximum = 110) for the 1, 5, and 10% concentrations, respectively. Based on this, the study authors considered sorbic acid as practically not irritating to the rabbit eye.
- Based on weight of evidence, a score of High was assigned. In a GLP-compliant OECD Guideline

405 ocular irritation test, neat sorbic acid was irritating to the eye with iris (score 1), conjunctival (score > 2), and corneal opacity (score ≥ 1) effects in 2 out of 3 animals with reversibility of irritative effects occurring within 21 days, meeting the GHS category 2A criteria (UN 2023). The second available ocular irritation study was reported with limited details and conducted on diluted sorbic acid. Therefore, it is not sufficient for classification purposes. ToxServices used the category 2A classification as the basis to assign a score of High.

Ecotoxicity (Ecotox)

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

Sorbic acid was assigned a score of Moderate for acute aquatic toxicity based on the measured L/EC_{50} values as low as 75 mg/L in fish (96-hr), 70 mg/L in daphnia (48-hr), and 41.9 mg/L in algae (72-hr) for the target chemical in guideline studies. GreenScreen® criteria classify chemicals as a Moderate hazard for acute aquatic toxicity when acute toxicity values are > 10 - 100 mg/L and when they are classified to GHS category 3 (CPA 2018b). The confidence in the score is high based on reliable, guideline studies for the target chemical for all three trophic levels.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2024a
  - 96-hr LC_{50} mortality (*Oryzias latipes*, fish) = 75 mg/L nominal (purity 99.5%, GLP-compliant, OECD Guideline 203) (Klimisch 1, reliable without restriction).
  - 48-hr EC_{50} mobility (*Daphnia magna*) = 70 mg/L nominal (purity 99.5%, GLP-compliant, OECD Guideline 202) (Klimisch 1, reliable without restriction).
  - 48-hr EC_{50} mobility (*D. magna*) = 353.54 mg/L nominal (purity > 99.5%, non-GLP-compliant, OECD Guideline 202) (Klimisch 2, reliable with restrictions).
  - 72-hr EC_{50} growth rate (*Raphidocelis subcapitata*) = 77 mg/L nominal, 72-hr EC_{50} biomass = 69 mg/L nominal (purity 99.5%, GLP-compliant, OECD Guideline 201) (Klimisch 1, reliable without restriction).
  - 72-hr EC_{50} growth rate (*Desmodesmus subspicatus*) = 41.9 mg/L measured, 72-hr EC_{50} biomass = 24.1 mg/L measured (purity not specified, GLP-compliant, OECD Guideline 201) (Klimisch 1, reliable without restriction).

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

Sorbic acid was assigned a score of Moderate for chronic aquatic toxicity based on the measured NOEC value of 6.47 mg/L in algae. GreenScreen® criteria classify chemicals as a Moderate hazard for acute aquatic toxicity when acute toxicity values are > 1 - 10 mg/L (CPA 2018b). The confidence in the score is low due to lack of measured data for fish for the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2024a
  - 21-day NOEC reproduction (*D. magna*) = 50 mg/L measured (purity 99.5%, GLP-compliant, OECD Guideline 211) (Klimisch 1, reliable without restriction).
  - 72-hr NOEC growth rate (*R. subcapitata*) = 56 mg/L nominal, 72-hr NOEC biomass = 32 mg/L nominal (purity 99.5%, GLP-compliant, OECD Guideline 201) (Klimisch 1, reliable without restriction).
  - 72-hr NOEC (*D. subspicatus*) = 6.47 mg/L measured (purity not specified, GLP-compliant,

OECD Guideline 201) (Klimisch 1, reliable without restriction).

- U.S. EPA 2022
  - Sorbic acid belongs to the Neutral Organics ECOSAR chemical class. The most conservative predicted chronic values (ChVs) are 189 mg/L in fish (freshwater) and 218 mg/L in fish (saltwater) (Appendix F).

Environmental Fate (Fate)

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

Sorbic acid was assigned a score of Very Low for persistence based on being readily biodegradable, meeting the 10-day window in an OECD Guideline 301 D ready biodegradability test. GreenScreen® criteria classify chemicals as a Very High Low hazard for persistence when they mainly partition to water, soil, or sediment, and meet the 10-day window in ready biodegradability studies (CPA 2018b). The confidence in the score is high based on reliable data for 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 2024a
  - A GLP-compliant ready biodegradability test conducted according to OECD 301 D (Ready Biodegradability: Closed Bottle Test) was performed with domestic activated sludge (adaptation not specified) exposed to sorbic acid (purity not specified) at 2 mg/L for 28 days. The degradation (based on O2 consumption) was 74.9% after 28 days and the 10-day window was reported as met. The authors of the REACH dossier concluded that the test substance was readily biodegradable (Klimisch 1, reliable without restriction).
- U.S. EPA 2017
  - The BIOWIN modeling Ready Biodegradable Predictor indicates that sorbic acid is expected to be readily biodegradable. Fugacity modeling (MCI method) predicts 63.6% will partition to soil with a half-life of 17.33 days, 36% will partition to water with a half-life of 8.67 days, and 0.0741% will partition to sediment with a half-life 77.92 days (Appendix G).

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

Sorbic acid was assigned a score of Very Low for bioaccumulation based on its measured log K_{ow} of -1.72 and modeled BCFs of 0.8944 and 3.162. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when the BCF/BAF is ≤ 100 and when log K_{ow} is ≤ 4 (CPA 2018b). The confidence in the score is high as it is based in part on measured log K_{ow} data on the target chemical, with support from modeling.

- 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
  - BCFBAF predicts a BCF of 3.162 using the regression-based model based on a measured log Kow of -1.72, and a BCF of 0.8944 using the Arnot-Gobas model for the upper trophic level, taking metabolism into consideration (Appendix G).
- ECHA 2024a
  - Sorbic acid has a log K_{ow} of 1.32 at pH = 2.5 and of -1.72 at pH = 6.5 as measured in a GLP-compliant OECD 117 test (Klimisch 1, reliable without restriction).

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *L*
Sorbic acid was assigned a score of Low for reactivity based on ToxServices not classifying it as a reactive chemical under GHS criteria based on screening evaluations conducted by the authors of the ECHA dossier. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when no GHS classification is available (CPA 2018b). The confidence in the score is low as it is not based on an authoritative list or measured data on the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2024a
  - The authors of the ECHA dossier reported that sorbic acid is not explosive based on a lack of functional groups related to explosion hazards as well as calculated thermodynamic properties (Klimisch 1, reliable without restriction).
  - The authors of the ECHA dossier reported that sorbic acid is not oxidizing based on a lack of functional groups related to oxidation hazards as well as calculated thermodynamic properties and negative oxygen balance (Klimisch 1, reliable without restriction).
- Based on the weight of evidence, ToxServices did not identify sorbic acid as reactive. Sorbic acid is not expected to be explosive, oxidizing, or self-reactive based on chemical structure analyses. It is not a peroxide. As it is not explosive, it does not require desensitization. Overall, sorbic acid is not classified for any of the reactivity sub endpoints under GHS (UN 2023). No data were found regarding corrosivity to metal.

Flammability (F) Score (vH, H, M, or L): L
Sorbic acid was assigned a score of Low for flammability based on ToxServices not classifying it as a flammable solid under GHS criteria based on results of flammability tests with the target chemical. GreenScreen® criteria classify chemicals as a Low hazard for flammability when no GHS classification is available (CPA 2018b). The confidence in the score is high as it is based on experimental data for the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2024a
  - Sorbic acid (purity 99.9%) was not flammable in an EU Method A.10 flammability test with no ignition achieved (Klimisch 1, reliable without restriction).
- Based on the above data, ToxServices did not classify sorbic acid as a flammable solid under GHS criteria (UN 2023).

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

New Approach Methodologies (NAMs) used in this GreenScreen® include *in silico* modeling for respiratory sensitization, chronic aquatic toxicity, persistence, and bioaccumulation, and *in vitro* testing for genotoxicity and endocrine activity. NAMs are non-animal alternative that can be used alone or in combination to provide information for safety assessment (Madden et al. 2020). At present, there is not a uniformly accepted framework on how to report and apply individual NAMs (U.S. EPA 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 5, Type I (input data) uncertainties in sorbic acid's NAMs dataset include no or insufficient experimental data for carcinogenicity, endocrine activity, and respiratory sensitization, and lack of established test methods for respiratory sensitization. Sorbic acid's Type II (extrapolation output) uncertainties include lack of defined applicability domains OECD QSAR Toolbox in examination of structural alerts, limitation of *in vitro* genotoxicity assays in mimicking *in vivo* metabolism and their focusing on one or only a few types of genotoxicity events, uncertain *in vivo* relevance of *in vitro* receptor binding activity assays, and the limitations in the examination of structural alerts for respiratory sensitization evaluation that does not account for non-immunologic mechanisms of respiratory sensitization. Some of sorbic acid's type II uncertainties were alleviated by the use of *in vitro* test batteries and/or in combination of *in vivo* data.

Table 4: Summary of NAMs Used in the GreenScreen® Assessment, Including Uncertainty Analyses	
Uncertainty Analyses (OECD 2020)	
Type I Uncertainty: Data/Model Input	**Carcinogenicity**: Only limited experimental data are available. **Genotoxicity:** The UDS assay method (OECD Guideline 482) has been deleted due to lack of use and poorer performance compared to other standard tests.[10] **Endocrine activity**: No *in vivo* data for hormone signaling pathways are available. **Respiratory sensitization**: No experimental data are available and there are no validated test methods. Very limited human evidence on aluminum compounds is confounded by co-exposure with other chemicals under occupational scenarios.
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

[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).
[10] https://www.oecd.org/env/ehs/testing/Draft_Intro_Genotoxicity%20TGs%20September%202014.pdf

	system does not entirely mimic *in vivo* conditions[11]. The *in vitro* UDS assay detects "longpatch repair" but is less sensitive for detection of "shortpatch repair". Mutagenic events may result from non-repair, misrepair, of misreplication of DNA lesions, and UDS gives no indication of fidelity of the repair process. It is possible that a mutagen interacts with DNA but damage is not repaired by an excision repair process.[12] **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. **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.	
Endpoint	**NAMs Data Available and Evaluated? (Y/N)**	**Types of NAMs Data (*in silico* modeling/*in vitro* biological profiling/frameworks)**
Carcinogenicity	N	
Mutagenicity	Y	*In vitro* data: Bacterial reverse mutation assay/*in vitro* UDS assay
Reproductive toxicity	N	
Developmental toxicity	N	
Endocrine activity	Y	*In vitro* high throughput data: EDSP Tox 21 screening assays
Acute mammalian toxicity	N	
Single exposure systemic toxicity	N	
Repeated exposure systemic toxicity	N	
Single exposure neurotoxicity	N	
Repeated exposure neurotoxicity	N	
Skin sensitization	N	
Respiratory sensitization	Y	*In silico* modeling: OECD Toolbox structural alerts
Skin irritation	N	
Eye irritation	N	
Acute aquatic toxicity	N	
Chronic aquatic toxicity	Y	*In silico* modeling: ECOSAR
Persistence	Y	*In silico* modeling: EPI Suite™

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

		Non-animal testing: OECD 301 D Biodegradation test
Bioaccumulation	Y	*In silico* modeling: EPI Suite™

References

Chemical Classification and Information Database (CCID). 2024. Sorbic acid (CAS #110-44-1). New Zealand Environmental Protection Authority. Available: https://www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/2643489B-1656-4B1F-8B6D-64525609725A

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

Cosmetic Ingredient Review (CIR). 1988. Final report on the safety assessment of sorbic acid and potassium sorbate. Washington, D.C.: Cosmetic Ingredient Review.

Djoumbou F.Y., R. Eisner, C. Knox, L. Chepelev, J. Hastings, G. Owen, E. Fahy, C. Steinbeck, S. Subramanian, E. Bolton, R. Greiner, and D.S. Wishart. 2016. ClassyFire: Automated Chemical Classification With A Comprehensive, Computable Taxonomy. J. Cheminformatics 2016(8):61. DOI: 10.1186/s13321-016-0174-y

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 (ECHA). 2024a. REACH dossier for hexa-2,4-dienoic acid (CAS #110-44-1. Available: https://echa.europa.eu/registration-dossier/-/registered-dossier/11476

European Chemicals Agency (ECHA). 2024b. C&L Inventory for hexa-2,4-dienoic acid (CAS #110-44-1. Available: https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/135653

European Commission (EC). 2024. CosIng Database. Available: https://ec.europa.eu/growth/tools-databases/cosing/

European Food Safety Authority (EFSA). 2015. Scientific Opinion on the re-evaluation of sorbic acid (E 200), potassium sorbate (E 202) and calcium sorbate (E 203) as food additives. *EFSA Journal* 13(6):4144. Available: https://efsa.onlinelibrary.wiley.com/doi/abs/10.2903/j.efsa.2015.4144

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/

European Food Safety Authority (EFSA). 2019. Opinion on the follow-up of the re-evaluation of sorbic acid (E200) and potassium sorbate (E202) as food additives. *EFSA Journal* 17(3):5625. Available: https://efsa.onlinelibrary.wiley.com/doi/abs/10.2903/j.efsa.2019.5625

Hazardous Substances Data Bank (HSDB). 2016. Sorbic acid (CAS# 110-44-1). United States National Library of Medicine. Available: https://pubchem.ncbi.nlm.nih.gov/source/hsdb/590

International Labour Organization (ILO). 1998. Ingredient chemical safety card (ICSC) for sorbic acid (CAS #110-44-1). ICSC #1284. Updated November 1998. Available: https://www.ilo.org/dyn/icsc/showcard.display?p_lang=en&p_card_id=1284&p_version=2

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

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). 2023. OECD QSAR Toolbox for Grouping Chemicals into Categories Version 4.6. Available: https://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm#Download_qsar_application_toolbox

Pharos. 2024. Pharos chemical and material library entry for sorbic acid (CAS #110-44-1). Available: https://pharosproject.net/chemicals/2004263

PubChem. 2024. Sorbic acid (CAS #110-44-1). United States National Library of Medicine. Available: https://pubchem.ncbi.nlm.nih.gov/compound/643460

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. Available: https://unece.org/transport/documents/2023/07/standards/ghs-rev10

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). 2015. Safer Choice Standard. Available: https://www.epa.gov/saferchoice/standard

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). 2023. Safer Chemical Ingredients List (SCIL). Available: https://www.epa.gov/saferchoice/safer-ingredients

United States Environmental Protection Agency (U.S. EPA). 2024. CompTox Dashboard. Available: https://comptox.epa.gov/dashboard

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 Sorbic Acid (CAS #110-44-1)

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
mical Details								S	R *	S	R *	*	*								
Chemical Name	CAS#	C	M	R	D	E	AT	STs	STr	Ns	Nr	SNS*	SNR*	IrS	IrE	AA	CA	P	B	Rx	F
Sorbic Acid	110-44-1	L	L	L	L	DG	L	L	L	*L*	L	*L*	*L*	L	H	M	*M*	vL	vL	*L*	L

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Sorbic Acid	3

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

Table 6

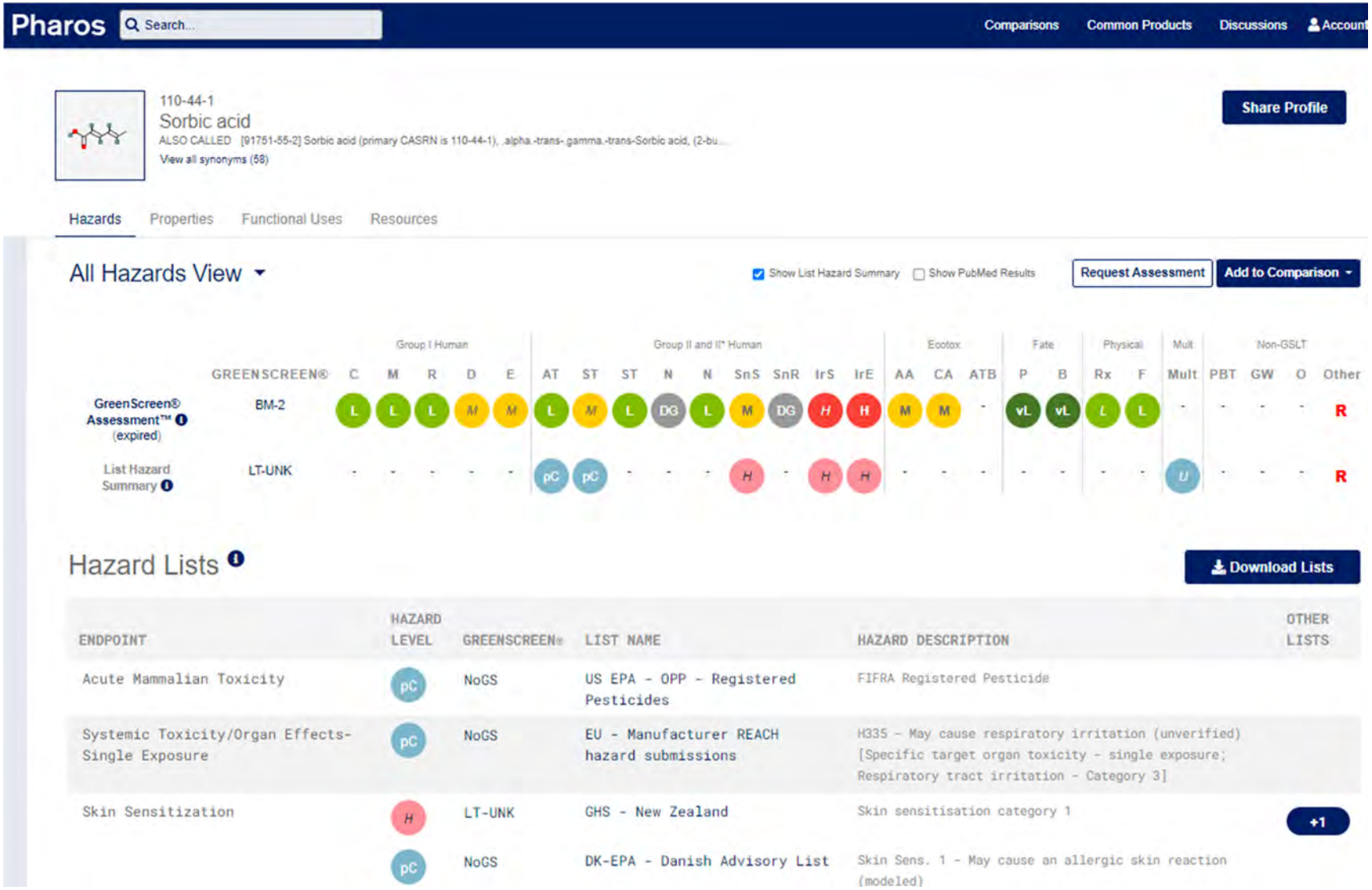
Chemical Name	Final GreenScreen® Benchmark Score
Sorbic Acid	3

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

Table 5: Data Gap Assessment Table

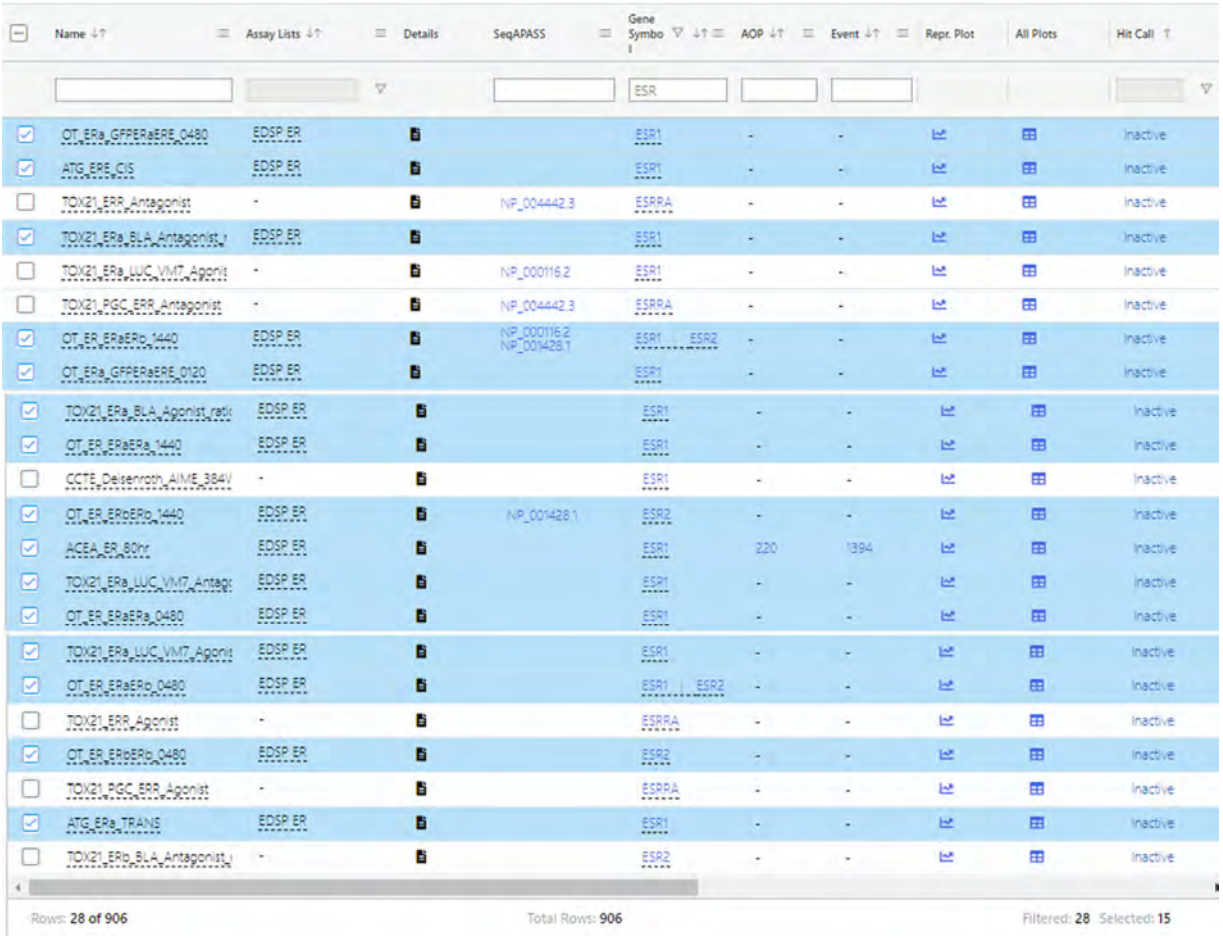
Datagap Criteria	a	b	c	d	e	f	g	h	i	j	bm4	End Result
1												
2												
3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes		3
4												

APPENDIX C: Pharos Output for Sorbic Acid (CAS #110-44-1)



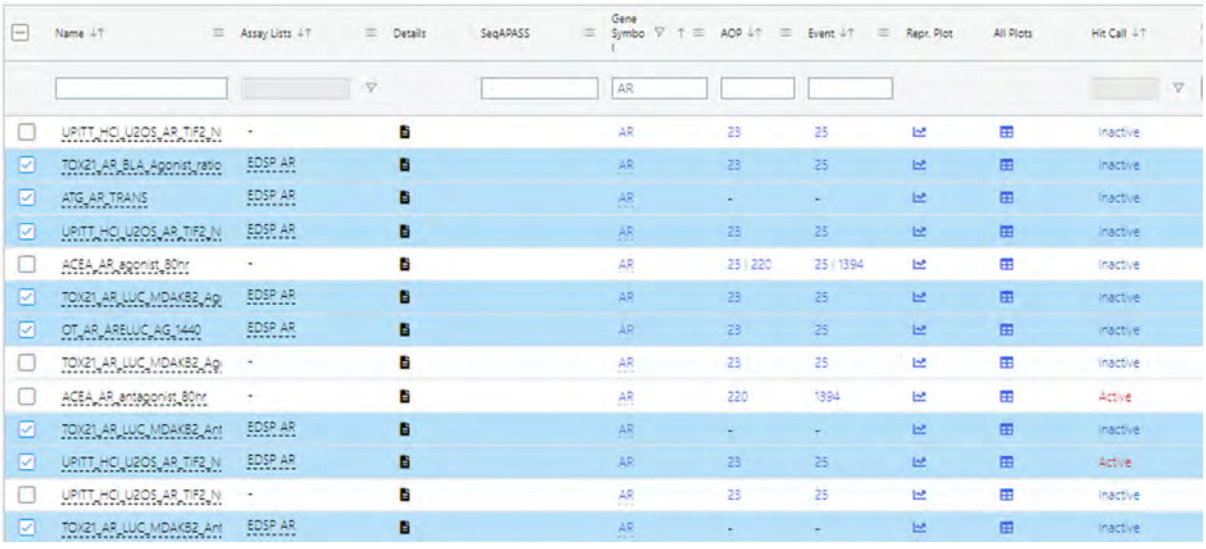
Skin Irritation/Corrosivity	H	LT-UNK	GHS - New Zealand	Skin irritation category 2	+3
	pC	NoGS	DK-EPA - Danish Advisory List	Skin Irrit. 2 - Causes skin irritation (modeled)	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H314 - Causes severe skin burns and eye damage (unverified) [Skin corrosion/irritation - Category 1A or 1B or 1C]	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H315 - Causes skin irritation (unverified) [Skin corrosion/irritation - Category 2]	
Eye Irritation/Corrosivity	H	LT-UNK	GHS - New Zealand	Eye irritation category 2	+1
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H319 - Causes serious eye irritation (unverified) [Serious eye damage/eye irritation - Category 2A]	
Human and/or Aquatic toxicity and/or Persistence and/or Bioaccumulation	U	LT-UNK	German FEA - Substances Hazardous to Waters	Class 1 - Low Hazard to Waters	

APPENDIX D: CompTox EDSP21 Results for Sorbic Acid (CAS #110-44-1)

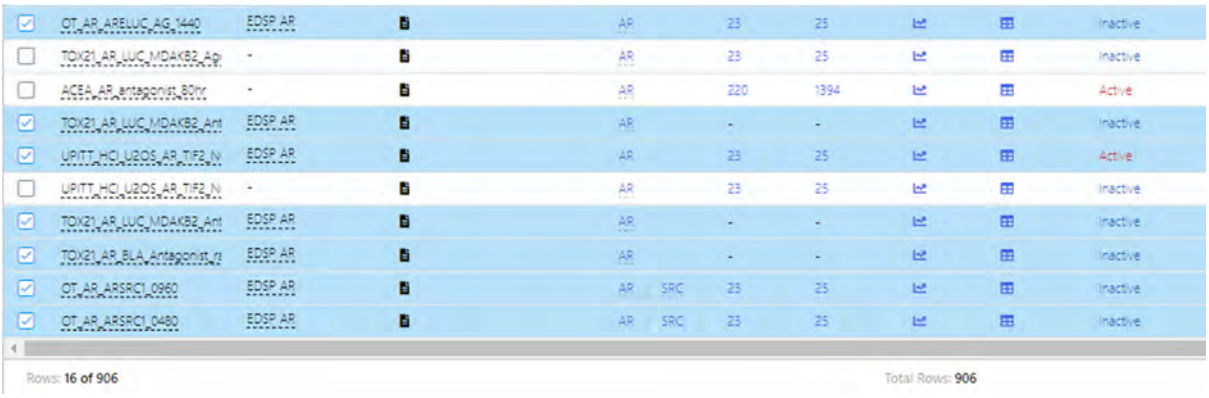


Name	Assay Lists	Details	SeqAPASS	Gene Symbol	AOP	Event	Repr. Plot	All Plots	Hit Call
				ESR					
OT_ERa_GFPERaERE_0480	EDSP ER			ESR1	-	-			Inactive
ATG_ERE_CIS	EDSP ER			ESR1	-	-			Inactive
TOX21_ERR_Antagonist	-		NP_004442.3	ESRRA	-	-			Inactive
TOX21_ERa_BLA_Antagonist_r	EDSP ER			ESR1	-	-			Inactive
TOX21_ERa_LUC_VM7_Agonist	-		NP_000116.2	ESR1	-	-			Inactive
TOX21_PGC_ERR_Antagonist	-		NP_004442.3	ESRRA	-	-			Inactive
OT_ER_ERaERb_1440	EDSP ER		NP_000116.2 NP_001428.1	ESR1 | ESR2	-	-			Inactive
OT_ERa_GFPERaERE_0120	EDSP ER			ESR1	-	-			Inactive
TOX21_ERa_BLA_Agonist_rati	EDSP ER			ESR1	-	-			Inactive
OT_ER_ERaERa_1440	EDSP ER			ESR1	-	-			Inactive
CCTE_Deisenroth_AIME_384V	-			ESR1	-	-			Inactive
OT_ER_ERbERb_1440	EDSP ER		NP_001428.1	ESR2	-	-			Inactive
ACEA_ER_80hr	EDSP ER			ESR1	220	1394			Inactive
TOX21_ERa_LUC_VM7_Antag	EDSP ER			ESR1	-	-			Inactive
OT_ER_ERaERa_0480	EDSP ER			ESR1	-	-			Inactive
TOX21_ERa_LUC_VM7_Agonist	EDSP ER			ESR1	-	-			Inactive
OT_ER_ERaERb_0480	EDSP ER			ESR1 | ESR2	-	-			Inactive
TOX21_ERR_Agonist	-			ESRRA	-	-			Inactive
OT_ER_ERbERb_0480	EDSP ER			ESR2	-	-			Inactive
TOX21_PGC_ERR_Agonist	-			ESRRA	-	-			Inactive
ATG_ERa_TRANS	EDSP ER			ESR1	-	-			Inactive
TOX21_ERb_BLA_Antagonist_r	-			ESR2	-	-			Inactive

Rows: 28 of 906 Total Rows: 906 Filtered: 28 Selected: 15

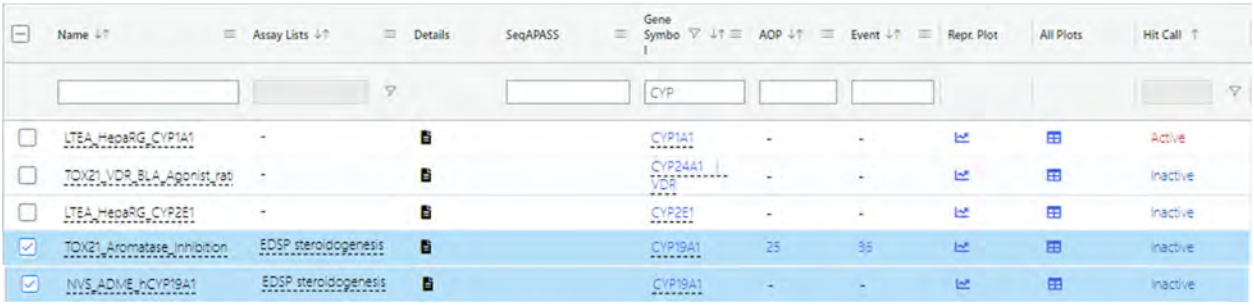


Name	Assay Lists	Details	SeqAPASS	Gene Symbol	AOP	Event	Repr. Plot	All Plots	Hit Call
				AR					
UPITT_HCI_U2OS_AR_TIF2_N	-			AR	23	25			Inactive
TOX21_AR_BLA_Agonist_ratio	EDSP AR			AR	23	25			Inactive
ATG_AR_TRANS	EDSP AR			AR	-	-			Inactive
UPITT_HCI_U2OS_AR_TIF2_N	EDSP AR			AR	23	25			Inactive
ACEA_AR_agonist_80hr	-			AR	23 | 220	25 | 1394			Inactive
TOX21_AR_LUC_MDAKB2_Ag	EDSP AR			AR	23	25			Inactive
OT_AR_ARELUC_AG_1440	EDSP AR			AR	23	25			Inactive
TOX21_AR_LUC_MDAKB2_Ag	-			AR	23	25			Inactive
ACEA_AR_antagonist_80hr	-			AR	220	1394			Active
TOX21_AR_LUC_MDAKB2_Ant	EDSP AR			AR	-	-			Inactive
UPITT_HCI_U2OS_AR_TIF2_N	EDSP AR			AR	23	25			Active
UPITT_HCI_U2OS_AR_TIF2_N	-			AR	23	25			Inactive
TOX21_AR_LUC_MDAKB2_Ant	EDSP AR			AR	-	-			Inactive

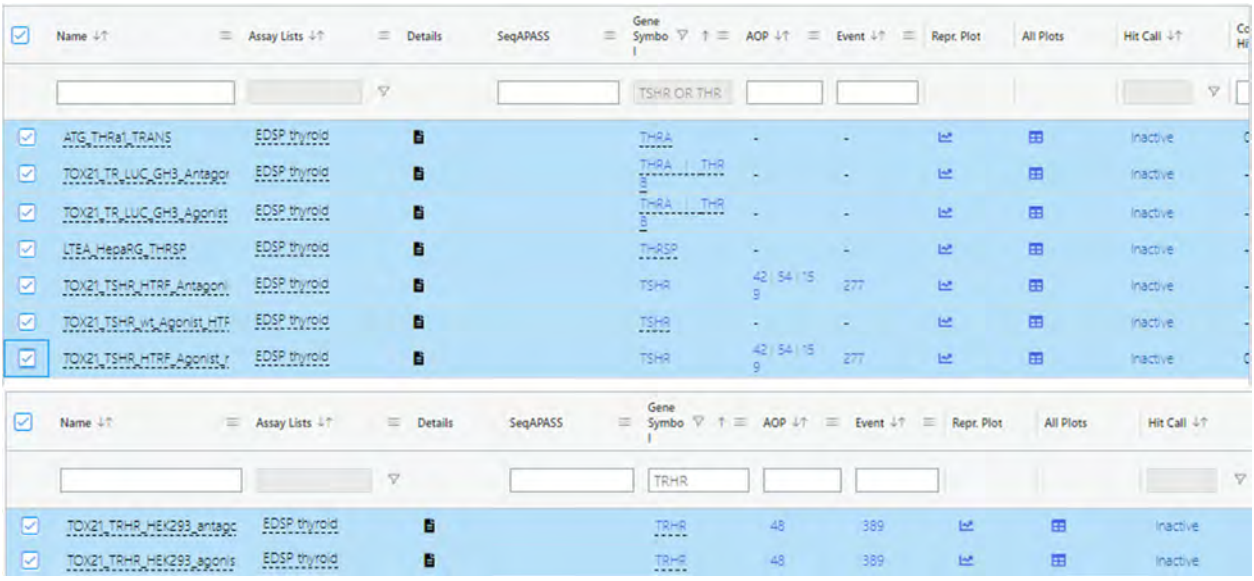


☑	OT_AR_ARELUC_AG_1440	EDSP AR		AR		23	25		Inactive
☐	TOX21_AR_LUC_MDAKB2_Ag	-		AR		23	25		Inactive
☐	ACEA_AR_antagonist_80hr	-		AR		220	1394		Active
☑	TOX21_AR_LUC_MDAKB2_Ant	EDSP AR		AR		-	-		Inactive
☑	UPITT_HCI_U2OS_AR_TIF2_N	EDSP AR		AR		23	25		Active
☐	UPITT_HCI_U2OS_AR_TIF2_N	-		AR		23	25		Inactive
☑	TOX21_AR_LUC_MDAKB2_Ant	EDSP AR		AR		-	-		Inactive
☑	TOX21_AR_BLA_Antagonist_r	EDSP AR		AR		-	-		Inactive
☑	OT_AR_ARSRC1_0960	EDSP AR		AR	SRC	23	25		Inactive
☑	OT_AR_ARSRC1_0480	EDSP AR		AR	SRC	23	25		Inactive

Rows: 16 of 906 Total Rows: 906



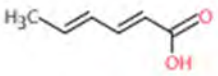
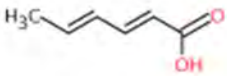
	Name	Assay Lists	Details	SeqAPASS	Gene Symbol	AOP	Event	Repr. Plot	All Plots	Hit Call
					CYP					
☐	LTEA_HepaRG_CYP1A1	-			CYP1A1	-	-			Active
☐	TOX21_VDR_BLA_Agonist_rat	-			CYP24A1 | VDR	-	-			Inactive
☐	LTEA_HepaRG_CYP2E1	-			CYP2E1	-	-			Inactive
☑	TOX21_Aromatase_Inhibition	EDSP steroidogenesis			CYP19A1	25	36			Inactive
☑	NVS_ADME_hCYP19A1	EDSP steroidogenesis			CYP19A1	-	-			Inactive



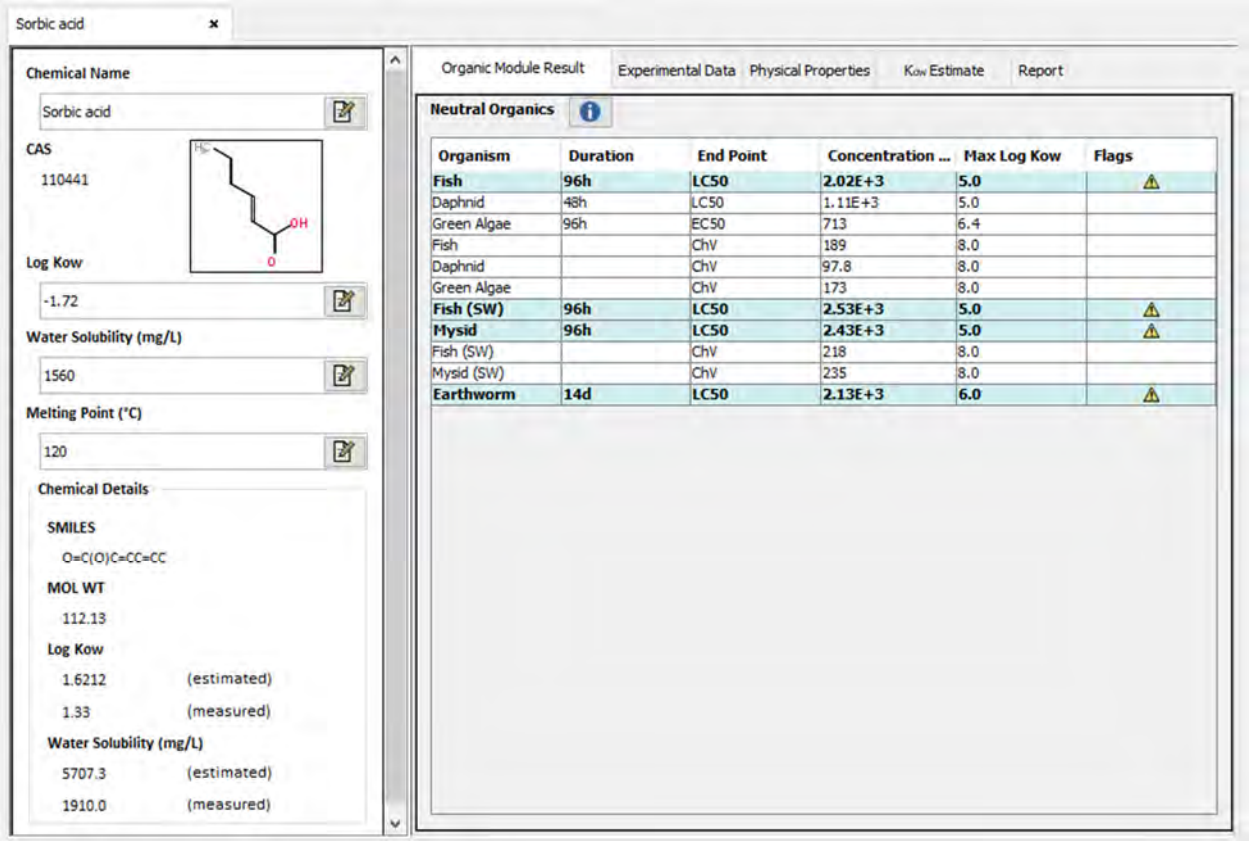
	Name	Assay Lists	Details	SeqAPASS	Gene Symbol	AOP	Event	Repr. Plot	All Plots	Hit Call
					TSHR OR THR					
☑	ATG_THRa1_TRANS	EDSP thyroid			THRA	-	-			Inactive
☑	TOX21_TR_LUC_GH3_Antagor	EDSP thyroid			THRA | THRB	-	-			Inactive
☑	TOX21_TR_LUC_GH3_Agonist	EDSP thyroid			THRA | THRB	-	-			Inactive
☑	LTEA_HepaRG_THRSP	EDSP thyroid			THRSP	-	-			Inactive
☑	TOX21_TSHR_HTRF_Antagoni	EDSP thyroid			TSHR	42 | 54 | 159	277			Inactive
☑	TOX21_TSHR_wt_Agonist_HTF	EDSP thyroid			TSHR	-	-			Inactive
☑	TOX21_TSHR_HTRF_Agonist_r	EDSP thyroid			TSHR	42 | 54 | 159	277			Inactive

	Name	Assay Lists	Details	SeqAPASS	Gene Symbol	AOP	Event	Repr. Plot	All Plots	Hit Call
					TRHR					
☑	TOX21_TRHR_HEK293_antago	EDSP thyroid			TRHR	48	389			Inactive
☑	TOX21_TRHR_HEK293_agonis	EDSP thyroid			TRHR	48	389			Inactive

APPENDIX E: OECD Respiratory Sensitization Results for Sorbic Acid (CAS #110-44-1)

Filter endpoint tree...	1	2
Structure		
Structure info		
Additional Ids	EC Number:2037687	EC Number:2037687
CAS Number	110-44-1	110-44-1
CAS-SMILES relation	High	Moderate
Chemical name(s)	_Sorbic_acid"""	(2e,4e)-hexa-2,4-dienoic acid
Identity	Sources:22	Sources:8
Molecular formula	C6H8O2	C6H8O2
Predefined substance type	Mono constituent	Mono constituent
SMILES	CC=CC=CC(O)=O	C\C=C\C=C\C(O)=O
Parameters		
Physical Chemical Properties		
Environmental Fate and Transport		
Ecotoxicological Information		
Human Health Hazards		
Profiling		
Predefined		
Database Affiliation	Acute Oral toxicity DB	Experimental pKa
Inventory Affiliation	AIIC	DSSTOX
OECD HPV Chemical Categories	Aliphatic acids	Aliphatic acids
Substance type	Discrete chemical	Discrete chemical
US-EPA New Chemical Categories	Not categorized	Not categorized
Endpoint Specific		
Respiratory sensitisation	No alert found	No alert found

APPENDIX F: ECOSAR Modeling Results for Sorbic Acid (CAS #110-44-1)

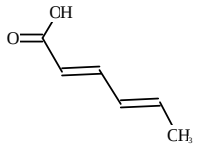


Organism	Duration	End Point	Concentration ...	Max Log Kow	Flags
Fish	**96h**	**LC50**	**2.02E+3**	**5.0**	⚠
Daphnid	48h	LC50	1.11E+3	5.0	
Green Algae	96h	EC50	713	6.4	
Fish		ChV	189	8.0	
Daphnid		ChV	97.8	8.0	
Green Algae		ChV	173	8.0	
Fish (SW)	**96h**	**LC50**	**2.53E+3**	**5.0**	⚠
Mysid	**96h**	**LC50**	**2.43E+3**	**5.0**	⚠
Fish (SW)		ChV	218	8.0	
Mysid (SW)		ChV	235	8.0	
Earthworm	**14d**	**LC50**	**2.13E+3**	**6.0**	⚠

APPENDIX G: EPI Suite™ Modeling Results for Sorbic Acid (CAS #110-44-1)

(Estimated values included in the C2C Screen are highlighted and bolded)

EPI Suite Results For CAS 110-44-1




```
CAS Number: 110-44-1
SMILES : O=C(O)C=CC=CC
CHEM   : 2,4-Hexadienoic acid, (E,E)-
MOL FOR: C6 H8 O2
MOL WT : 112.13
------------------------------ EPI SUMMARY (v4.11) --------------------------
 Physical Property Inputs:
    Log Kow (octanol-water):   -1.72
    Boiling Point (deg C)  :   ------
    Melting Point (deg C)  :   120.00
    Vapor Pressure (mm Hg) :   ------
    Water Solubility (mg/L):   1560
    Henry LC (atm-m3/mole) :   ------

 Log Octanol-Water Partition Coef (SRC):
    Log Kow (KOWWIN v1.69 estimate) =  1.62
    Log Kow (Exper. database match) =  1.33
       Exper. Ref:  HANSCH,C ET AL. (1995)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
    Boiling Pt (deg C):  219.63  (Adapted Stein & Brown method)
    Melting Pt (deg C):  24.62  (Mean or Weighted MP)
    VP(mm Hg,25 deg C):  0.0142  (Modified Grain method)
    VP (Pa, 25 deg C) :  1.89  (Modified Grain method)
    MP  (exp database):  134.5 deg C
    Subcooled liquid VP: 0.124 mm Hg (25 deg C, Mod-Grain method)
                       : 16.6 Pa (25 deg C, Mod-Grain method)

 Water Solubility Estimate from Log Kow (WSKOW v1.42):
    Water Solubility at 25 deg C (mg/L):  1e+006
       log Kow used: -1.72 (user entered)
       melt pt used: 120.00 deg C
     Water Sol (Exper. database match) =  1910 mg/L (30 deg C)
        Exper. Ref:  YALKOWSKY,SH & DANNENFELSER,RM (1992)

 Water Sol Estimate from Fragments:
```

```
    Wat Sol (v1.01 est) =  9636 mg/L

 ECOSAR Class Program (ECOSAR v1.11):
    Class(es) found:
       Neutral Organics-acid

 Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
   Bond Method :   5.72E-007  atm-m3/mole  (5.79E-002 Pa-m3/mole)
   Group Method:   4.99E-008  atm-m3/mole  (5.06E-003 Pa-m3/mole)
 For Henry LC Comparison Purposes:
   User-Entered Henry LC:  not entered
   Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
      HLC:  1.343E-006 atm-m3/mole  (1.361E-001 Pa-m3/mole)
      VP:   0.0142 mm Hg (source: MPBPVP)
      WS:   1.56E+003 mg/L (source: User-Entered)

 Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
  Log Kow used:  -1.72  (user entered)
  Log Kaw used:  -4.631  (HenryWin est)
      Log Koa (KOAWIN v1.10 estimate):  2.911
      Log Koa (experimental database):  None

 Probability of Rapid Biodegradation (BIOWIN v4.10):
   Biowin1 (Linear Model)         :   0.8753
   Biowin2 (Non-Linear Model)     :   0.9802
 Expert Survey Biodegradation Results:
   Biowin3 (Ultimate Survey Model):   3.6143  (days-weeks  )
   Biowin4 (Primary Survey Model) :   4.3406  (hours-days  )
 MITI Biodegradation Probability:
   Biowin5 (MITI Linear Model)    :   0.7103
   Biowin6 (MITI Non-Linear Model):   0.8427
 Anaerobic Biodegradation Probability:
   Biowin7 (Anaerobic Linear Model):  0.3315
 Ready Biodegradability Prediction:   YES

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

 Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
  Vapor pressure (liquid/subcooled):  16.5 Pa (0.124 mm Hg)
  Log Koa (Koawin est  ): 2.911
   Kp (particle/gas partition coef. (m3/ug)):
       Mackay model           :  1.81E-007
       Octanol/air (Koa) model:  2E-010
   Fraction sorbed to airborne particulates (phi):
       Junge-Pankow model     :  6.55E-006
       Mackay model           :  1.45E-005
       Octanol/air (Koa) model:  1.6E-008

 Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
   Hydroxyl Radicals Reaction:
      OVERALL OH Rate Constant =  50.3560 E-12 cm3/molecule-sec
      Half-Life =     0.212 Days (12-hr day; 1.5E6 OH/cm3)
      Half-Life =     2.549 Hrs
   Ozone Reaction:
      OVERALL Ozone Rate Constant =     5.265000 E-17 cm3/molecule-sec
      Half-Life =     0.218 Days (at 7E11 mol/cm3)
```

```
      Half-Life =      5.224 Hrs
   Fraction sorbed to airborne particulates (phi):
      1.05E-005 (Junge-Pankow, Mackay avg)
      1.6E-008 (Koa method)
    Note: the sorbed fraction may be resistant to atmospheric oxidation

 Soil Adsorption Coefficient (KOCWIN v2.00):
      Koc    :  8.715  L/kg (MCI method)
      Log Koc:  0.940       (MCI method)
      Koc    :  0.1601  L/kg (Kow method)
      Log Koc:  -0.796      (Kow method)

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

 Bioaccumulation Estimates (BCFBAF v3.01):
   Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
   Log Biotransformation Half-life (HL) = -1.2983 days (HL = 0.05031 days)
   Log BCF Arnot-Gobas method (upper trophic) = -0.048 (BCF = 0.8944)
   Log BAF Arnot-Gobas method (upper trophic) = -0.048 (BAF = 0.8944)
        log Kow used: -1.72 (user entered)

 Volatilization from Water:
    Henry LC:  4.99E-008 atm-m3/mole  (estimated by Group SAR Method)
    Half-Life from Model River: 1.243E+004  hours   (517.7 days)
    Half-Life from Model Lake : 1.356E+005  hours   (5652 days)

 Removal In Wastewater Treatment:
    Total removal:               1.85  percent
    Total biodegradation:        0.09  percent
    Total sludge adsorption:     1.75  percent
    Total to Air:                0.00  percent
      (using 10000 hr Bio P,A,S)

 Level III Fugacity Model: (MCI Method)
             Mass Amount    Half-Life    Emissions
              (percent)       (hr)       (kg/hr)
   Air        0.381          2.58         1000
   Water      36             208          1000
   Soil       63.6           416          1000
   Sediment   0.0741         1.87e+003    0
     Persistence Time: 272 hr

 Level III Fugacity Model: (MCI Method with Water percents)
             Mass Amount    Half-Life    Emissions
              (percent)       (hr)       (kg/hr)
   Air        0.381          2.58         1000
   Water      36             208          1000
     water      (36)
     biota      (3.43e-008)
     suspended sediment (0.00047)
   Soil       63.6           416          1000
   Sediment   0.0741         1.87e+003    0
     Persistence Time: 272 hr

 Level III Fugacity Model: (EQC Default)
             Mass Amount    Half-Life    Emissions
```

```
           (percent)        (hr)       (kg/hr)
   Air       0.409           2.58         1000
   Water     41.7            208          1000
     water     (41.7)
     biota     (3.97e-008)
     suspended sediment (4.89e-007)
   Soil      57.8            416          1000
   Sediment  0.0722          1.87e+003    0
     Persistence Time: 256 hr
```

APPENDIX H: Change in Benchmark Score

Table 5 provides a summary of changes to the GreenScreen® Benchmark™ for sorbic acid. The GreenScreen® Benchmark Score for sorbic acid has changed over time. The original GreenScreen® assessment was performed in 2015 under version 1.2 criteria and ToxServices assigned a Benchmark 3 (BM-3) score. The BM-3 score was maintained with a version 1.4 update in 2024; however, there was a reclassification of a number of endpoints following a weight of evidence evaluation of this chemical's current dataset (Appendix H).

Table 5: Change in GreenScreen® Benchmark™ for Sorbic Acid

Date	GreenScreen® Benchmark™	GreenScreen® Version	Comment
April 8, 2015	BM-3	v. 1.2	Original report.
February 22, 2024	BM-3	v. 1.4	The GreenScreen® assessment was updated with a v.1.4 template. No change in BM score; however, there was a reclassification of a number of endpoints, including the systemic toxicity – single dose endpoint from *Moderate* (Low confidence) to *Low* (High confidence), the neurotoxicity – single exposure endpoint from *Data Gap* to *Low* (Low confidence), the skin sensitization endpoint from *Moderate* (Low confidence) to *Low* (Low confidence), the respiratory sensitization endpoints from *Data Gap* to *Low* (Low confidence), the skin irritation endpoint from *High* (Low confidence) to *Low* (High confidence), and the aquatic acute toxicity endpoint from *Moderate* (High confidence) to *Moderate* (Low confidence).

Licensed GreenScreen® Profilers

Sorbic Acid GreenScreen® Evaluation Prepared by:

SIGNATURE BLOCK

Deb Remeikas, M.A.
Toxicologist
ToxServices LLC

Sorbic Acid GreenScreen® Evaluation QC'd by:

SIGNATURE BLOCK

Jennifer Rutkiewicz, Ph.D.
Senior Toxicologist
ToxServices LLC