SULFURIC ACID, MONO-C12-18-ALKYL ESTERS, SODIUM SALTS / SODIUM PENTADECYL SULFATE / SODIUM COCO SULFATE

(CAS #68955-19-1)

GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

ToxServices LLC

Assessment Date: May 28, 2021

Expiration Date: May 28, 2026

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING
1367 Connecticut Ave., N.W., Suite 300
Washington, D.C. 20036

TABLE OF CONTENTS

TABLE OF FIGURES

TABLE OF TABLES

GreenScreen® Executive Summary for Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate (CAS #68955-19-1)

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate are sodium salts of alkyl alcohol sulfates. The substance consists of a mixture of carbon chains with lengths of C12-18, but mainly C12. Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate function primarily as an ionic surfactant, but also functions as a cleansing and foaming agent in personal care and cosmetic products. Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is a white powdery solid that has high water solubility and low volatility. It is non-reactive but is classified as a GHS Category 2 flammable solid.

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes"). This score is based on the following hazard score combinations:

- Benchmark 2f
    - Very High Group II Human Health Hazard (eye irritation-IrE)

Data gaps (DG) exist for reproductive toxicity-R, endocrine activity-E, and neurotoxicity-Nr* (repeated dose). As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gaps. In a worst-case scenario, if sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate were assigned a High score for the data gaps R or E, it would be categorized as a Benchmark 1 Chemical.

New Approach Methodologies (NAMs) used in this GreenScreen® include *in vitro* genotoxicity assays, *in vitro* and *in silico* endocrine activity assessments, and use of structural alerts to evaluate respiratory sensitization. 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 Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate's NAMs dataset include no experimental data for endocrine activity and respiratory sensitization. Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate's Type II (extrapolation output) uncertainties include limitations in the applicability domains of the (Quantitative) Structure Activity Relationship ((Q)SAR) models applied in this assessment and exogenous metabolic systems used in *in vitro* genotoxicity tests that do not entirely mirror *in vivo* metabolism. Some of sodium lauryl sulfate and C10-C16 alkyl alcohol sulfuric acid, sodium salt's type II uncertainties were alleviated by the use of *in vitro* test batteries in combination of *in vivo* data.

GreenScreen® Hazard Summary Table for Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate

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

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 Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate (CAS #68955-19-1)

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

GreenScreen® Assessment (v.1.4) Prepared By:
Name: Zach Guerrette, Ph.D., D.A.B.T.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: April 23, 2021; May 28, 2021

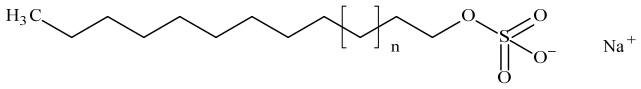
Quality Control Performed By:
Name: Bingxuan Wang, Ph.D., D.A.B.T.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: April 27, 2021; May 28, 2021

Expiration Date: May 28, 2026[2]

Chemical Name: Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate

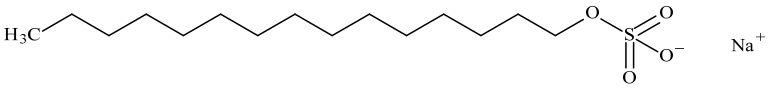
CAS Number: 68955-19-1

Chemical Structure(s):



Where n = 1-7

Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts



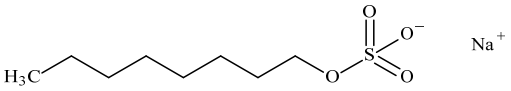
Sodium Pentadecyl Sulfate

Also called:
Sodium pentadecyl sulfate; Sulfuric acid, mono-C12-18-alkyl esters, sodium salts; Sodium pentadecylsulfate; CAS #13393-71-0; Pentadecyl sodium sulfate; Sodium pentadecyl sulphate; EC 236-475-8; EC 273-257-1; sodium C12-18 alkyl sulfate; sodium;pentadecyl sulfate; Sulfuric acid sodium pentadecyl (ChemIDplus 2021, PubChem 2021)

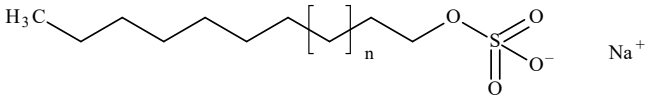
Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):
ToxServices identified data gaps for sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate. Therefore, Toxservices included data for related alkyl alcohol sulfuric acid, sodium salts, some of which are constituents of sulfuric acid, mono-C12-18-alkyl esters,

[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).

sodium salts and magnesium, ammonium, and potassium salts of related alkyl sulfates. ToxServices does not expect the potassium, ammonium, or magnesium cation to have greater toxicity that the sodium cation.

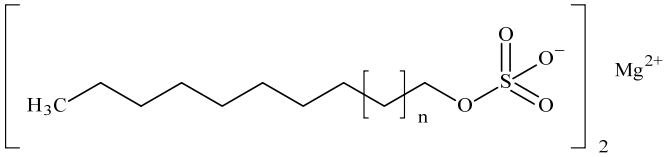


Surrogate: Sodium octyl sulfate (CAS #142-31-4)



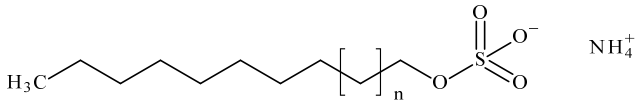
Where n = 1-7.

Surrogate: Sulfuric acid, mono-C10-16-alkyl esters, sodium salts (CAS #68585-47-7)

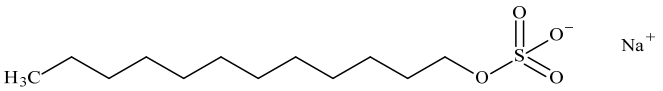


Where n = 1-7

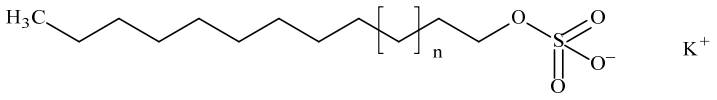
Surrogate: Sulfuric acid, mono-C10-16-alkyl esters, magnesium salts (CAS #68081-97-0)



Surrogate: Sulfuric acid, mono-C10-16-alkyl esters, ammonium salts (CAS #68081-96-9)

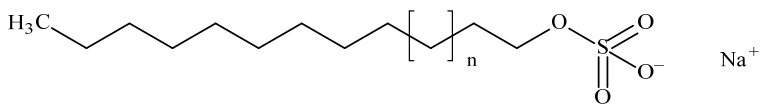


Surrogate: Sodium lauryl sulfate / sodium dodecyl sulfate (CAS #151-21-3)



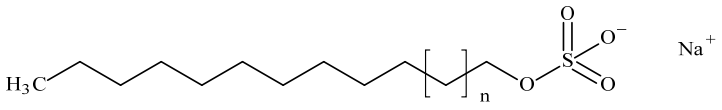
Where n = 1 or 2

Surrogate: Sulfuric acid, mono-C12-13-alkyl esters, potassium salts (CAS #91783-22-1)



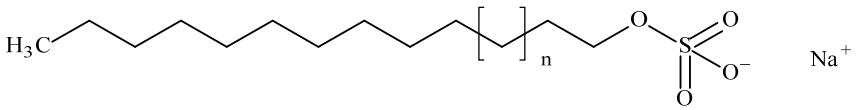
Where n = 1-4

Surrogate: Sulfuric acid, mono-C12-15-alkyl esters, sodium salts (CAS #68890-70-0)



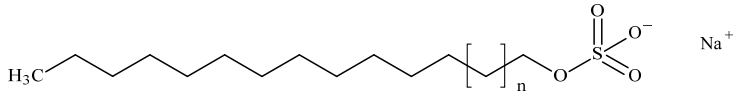
Where n = 1-5

Surrogate: Sulfuric acid, mono-C12-16-alkyl esters, sodium salts (CAS #73296-89-6)



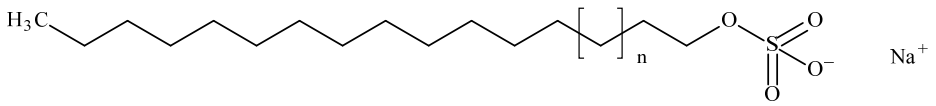
Where n = 1-3

Surrogate: Sulfuric Acid, Mono-C13-15-alkyl esters, sodium salts (CAS #86014-79-1)



Where n = 1-5

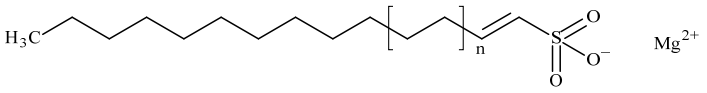
Surrogate: Sulfuric acid, mono-C14-18-alkyl esters, sodium salts (CAS #68081-98-1)



Where n = 1-3

Surrogate: Sulfuric acid, mono-C16-18-alkyl esters, sodium salts (CAS #68955-20-4)

Finally, to address the lack of reprodutive toxicity studies for alkyl sulfates, ToxServices used data for a mixture of C14:C16:C18 (1:1:1 ratio) α-olefin sulfonate, magnesium salt (CAS #N/A) to fill the data gap. Sulfates have an oxygen atom between the sulfur atom and the alkyl chain, whereas the alkyl chains of sulfonates are directly bonded to the sulfur atom. Additionally, α-olefin sulfonates have a double bond at the initial (alpha) carbon attached to the sulfur atom, and sulfonates. Despite these differences, ToxServices considered α-olefin sulfonates to be suitable surrogates for alkyl sulfates due to their shared structural elements (aklyl chains connected to a sulfur-based acid moieity) and surfactant properties.



Surrogate: Mixture of C14:C16:C18 (1:1:1 ratio) α-olefin sulfonate, magnesium salt (CAS #N/A)

Identify Applications/Functional Uses (OECD 2009, EC 2021)**:**
1. Ionic surfactant.
2. Cleansing and foaming agent, and surfactant (emulsifying and/or cleansing) in cosmetics and personal care products.

Known Impurities[3]:
Commercial alkyl sulfate products contain sodium sulfate and residual alcohols (OECD 2009). The screen is performed on the theoretical pure substance.

GreenScreen® Summary Rating for Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate[4,5 6,7]: Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes") (CPA 2018b). This score is based on the following hazard score combinations:

- Benchmark 2f
    - Very High Group II Human Health Hazard (eye irritation-IrE)

Data gaps (DG) exist for reproductive toxicity-R, endocrine activity-E, and neurotoxicity-Nr* (repeated dose). As outlined in GreenScreen® Guidance (CPA 2018b) Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gaps. In a worst-case scenario, if sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate were assigned a High score for the data gaps R or E, it would be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Summary Table for Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate

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

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 sulfuric acid, mono-C12-18-alkyl esters, sodium salts /

[3] Impurities of the chemical will be assessed at the product level instead of in this GreenScreen®.
[4] For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.
[5] See Appendix A for a glossary of hazard endpoint acronyms.
[6] For inorganic chemicals only, see GreenScreen® Guidance v1.4 Section 12 (Inorganic Chemical Assessment Procedure).
[7] For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen® Guidance v1.4 Annex 2.

sodium pentadecyl sulfate / sodium coco sulfate is readily biodegradable (ECHA 2021a), it is not expected to have relevant transformation products.

Introduction

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate consists of a mixture of alkyl sulfates, with a typical composition of 48-58% C12, 18-24% C14, 8-12% C16, and 11-15% C18 (OECD 2009). Alkyl sulfates function primarily as ionic surfactants. Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate functions as a cleansing and foaming agent and a surfactant (cleansing and/or emulsifying) in cosmetics and personal care products (EC 2021). Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is produced via sulfation of the primary alcohols with sulfur trioxide or chlorosulfonic acid and subsequent neutralization with a base (sodium hydroxide) (OECD 2009).

ToxServices assessed sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate against GreenScreen® Version 1.4 (CPA 2018b) following procedures outlined in ToxServices' SOPs (GreenScreen® Hazard Assessment) (ToxServices 2020).

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

The SCIL is a list of chemicals that meet the Safer Choice standard (U.S. EPA 2020a). It can be accessed at: http://www2.epa.gov/saferchoice/safer-ingredients. Chemicals on the SCIL have been assessed for compliance with the Safer Choice Standard and Criteria for Safer Chemical Ingredients (U.S. EPA 2015).

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is listed on the U.S. EPA SCIL as a surfactant with a full green circle.

GreenScreen® List Translator Screening Results

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen Benchmark™ 1 chemicals (CPA 2018b). Pharos (Pharos 2021) is an online list-searching tool that is used to screen chemicals against all of the lists in the List Translator electronically. ToxServices also checks the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b),[8] which are not considered GreenScreen® Specified Lists but are additional information sources, in conjunction with the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate can be found in Appendix C.

- Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is an LT-P1 chemical when screened using Pharos, and therefore a full GreenScreen® is required.
- Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is not listed on the U.S. DOT list.
- Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is on the following list for multiple endpoints:
    - German FEA - Substances Hazardous to Waters - Class 2 - Hazard to Waters

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

- Specified lists for single endpoints are reported in individual hazard endpoints in the hazard assessment section below.

Hazard Statement and Occupational Control

Globally Harmonized Systems of Classification and Labelling of Chemicals (GHS) classifications that are harmonized across European Union (EU) are not available for sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate. The authors of the REACH dossier have classified it as a GHS Category 2 skin irritant (H315), a GHS Category 2 eye irritant (H318), and a GHS Category 3 chronic aquatic toxicant (H412) (ECHA 2021a). These hazard statements are presented in Table 1.

Table 1: GHS H Statements for Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate (CAS #68955-19-1) (ECHA 2021a)

H Statement	H Statement Details
H315	Causes skin irritation.
H318	Causes serious eye damage.
H412	Harmful to aquatic life with long lasting effects.

General personal protective equipment (PPE) recommendations are presented in Table 2, below. No occupational exposure limits (OELs) were identified for sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate.

Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate (CAS #68955-19-1)

Personal Protective Equipment (PPE)	Reference	Occupational Exposure Limits (OEL)	Reference
Gloves, goggles, protective clothing, suitable breathing mask	ECHA 2021a	None identified	OSHA 2021

Physicochemical Properties of Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is a white, powdery solid under standard temperature and pressure. It is not expected to be significantly volatile based on a vapor pressure no greater than 0.135 mm Hg. It is highly soluble in water (> 250,000 mg/L).

Table 3: Physical and Chemical Properties of Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate (CAS #68955-19-1)

Property	Value	Reference
Molecular formula	C15H31NaO4S (representative structure)	PubChem 2021
SMILES Notation	Representative structures: [Na+].CCCCCCCCCCCCCCCCOS(=O)(=O)[O-] CCCCCCCCCCCCCCCCOS(=O)(=O)[O-].[Na+]	ChemIDplus 2021 PubChem 2021
Molecular weight	330.4619 g/mol 330.5 g/mol	ChemIDplus 2021 PubChem 2021

Table 3: Physical and Chemical Properties of Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate (CAS #68955-19-1)		
Property	**Value**	**Reference**
Physical state	Solid	ECHA 2021a
Appearance	White, powdery	ECHA 2021a
Melting point	-3°C (glass transition temperature), 36°C (melting of crystalline parts) (OECD 102)	ECHA 2021a
Boiling point	208°C (demonstrated initial boiling followed by decomposition) (OECD 103)	ECHA 2021a
Vapor pressure	≤ 18 Pa (≤ 0.135 mm Hg) at 20°C	ECHA 2021a
Water solubility	> 250 g/L (> 250,000 mg/L) at 20°C (OECD 105)	ECHA 2021a
Dissociation constant	pKa = 2.15 at 2°C0 (OECD 112)	ECHA 2021a
Density/specific gravity	Bulk density = 605 g/L (DGF H-II 1B (92) (by 3.1))	ECHA 2021a
Partition coefficient	Log K_{ow} ≤ -2.1 at 20°C (calculated) (OECD 107) Log K_{ow} = 1.41 at 24°C (OECD 123)	ECHA 2021a

Toxicokinetics

ToxServices identified no toxicokinetic data specifically for sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate. Data for alkyl sulfate salts are discussed below.

Absorption:

Following oral dosing, alkyl sulfate salts are significantly absorbed from the gastrointestinal tract of rats, dogs, and humans, with up to 98% (≤ 98%) of administered sodium lauryl sulfate excreted in the urine. In contrast, absorption across intact skin is limited since anionic surfactants have a binding affinity for skin surfaces (OECD 2009). ToxServices identified no data for inhalation absorption.

Distribution:

Plasma concentrations of radiolabeled C16 alkyl alcohol sulfuric acid, erythromycin salt peaked 0.5-2 hours following oral dosing in dogs and humans and then declined rapidly, with 10% of the maximum concentration achieved after 6 hours. Whole body autoradiography following intraperitoneal injection of rats with ^{35}S-radio labeled C10, C12, or C18 alkyl alcohol sulfuric acid, potassium salts indicated that only the liver and kidney exhibited measurable radioactivity. The radioactivity levels were highest one hour after dosing and cleared most rapidly for the C10 salt (OECD 2009).

Metabolism:

Rats, dogs, and humans extensively metabolize alkyl sulfates via ω- and β-oxidation to yield metabolites containing C2 and C4 alkyl chains, including butyric acid 4-sulfate (CAS #16899-85-7) and 4-butyrolactone (CAS #96-48-0), for even-numbered alkyl chain sulfates. Glycolic acid sulfate (CAS #N/A) has also been identified as a minor metabolite in the dog and human urine. For odd-numbered alkyl sulfates, specifically the C11 alkyl sulfate, propionic acid-3-sulfate (CAS #N/A), pentanoic acid-5-

sulfate (CAS #N/A), and inorganic sulfate (CAS #14808-79-8) were identified as metabolites and were postulated to be produced via ω- and β-oxidation. The C2 alkyl chain metabolites are utilized by the body in energy production pathways, and ultimately eliminated from the body as carbon dioxide (OECD 2009).

Excretion:

The major route of elimination for alkyl sulfates and their metabolites is via the urine. Overall excretion rates do not differ between male and female rats, but alkyl sulfates of differing alkyl chain length exhibit different urinary excretion rates, with lauryl sulfates having faster elimination than C10, C11, or C18 chains following intraperitoneal or oral administration. This suggests that the lauryl sulfates are metabolized more rapidly than other alkyl sulfates. Fecal elimination occurs to a lesser extent and accounts for ≤ 19.9% of total excretion (OECD 2009).

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M, or L): L
Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Low for carcinogenicity based on the lack of tumorigenicity identified for the surrogate sulfuric acid, mono-C12-15-alkyl esters, sodium salts. 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 measured data on a strong surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
  - *Oral: Surrogate: Sulfuric acid, mono-C12-15-alkyl esters, sodium salts (CAS #68890-70-0)*: A pre-GLP combined chronic toxicity/carcinogenicity study conducted in a manner similar to OECD Guideline 453 (missing some examinations like urinalysis parameters) was performed with Colworth Wistar rats (45/sex/group) provided diets containing the surrogate sulfuric acid, mono-C12-15-alkyl esters, sodium salts (purity not specified) at 0.015, 0.15, or 1.5% (contributing doses of 11, 113, and 1,125 mg/kg/day, respectively) for two years. Treatment did not increase the total number of tumors, the number of tumor-bearing rats, or the tumor incidence. While the total number of pancreatic tumors was increased in high dose males, this was due to a slight increase in both islet- and exocrine-type tumors. When analyzed separately, no statistically significant difference was detected between the treatment and control groups. The REACH dossier authors concluded that the surrogate sulfuric acid, mono-C12-15-alkyl esters, sodium salts was not carcinogenic under the conditions of this test (Klimisch Score 2, reliable with restrictions).

Mutagenicity/Genotoxicity (M) Score (H, M, or L): L
Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Low for mutagenicity/genotoxicity based on negative results for mutagenicity and clastogenicity in a battery of *in vitro* and *in vivo* studies of alkyl sulfates. 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 measured data on the target substance and strong surrogates.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
  - *In vitro*: A GLP-compliant bacterial reverse mutation assay conducted in a manner similar to OECD Guideline 471 (no *S. typhimurium* TA102 or *E. coli* strain tested) was performed with *Salmonella typhimurium* tester strains TA1535, TA1537, TA98, TA100, and TA1538 exposed to sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (39.4% active ingredient) in water at ≤ 5,000 µg/plate with and without exogenous metabolic activation (unspecified S9 mix). Cytotoxicity was evident at ≥ 200 µg/plate with and without metabolic activation. Treatment did not increase the mutation frequency in the presence or absence of metabolic activation. The authors indicated that the vehicle and positive (sodium azide, 9-aminoacridine, 4-nitroquinoline-N-oxide, and 2-aminoanthracene) controls were valid (Klimisch Score 2, reliable with restrictions).
  - *In vitro*: *Surrogate: Sodium lauryl sulfate (CAS #151-21-3):* A non-GLP-compliant mammalian cell gene mutation assay conducted in a manner similar to OECD Guideline 476 was performed with mouse lymphoma L5178Y cells exposed to sodium lauryl sulfate (purity not specified) in dimethyl sulfoxide (DMSO) at ≤ 100 µg/mL without and ≤ 95 µg/mL with exogenous metabolic activation (S9 mix prepared from livers of male Fischer 344 rats induced with Aroclor 1254). Cytotoxicity was evident at concentrations ≥ 70 µg/mL without and at 95 µg/mL with metabolic activation. Treatment did not increase the mutation frequency in the presence or absence of metabolic activation. The authors indicated the vehicle and positive (3-methylcholanthrene, methylmethanesulfonate) were valid (Klimisch Score 2, reliable with restrictions).
  - *In vivo: Surrogate: Sulfuric acid, mono-C16-18-alkyl esters, sodium salts (CAS #68955-20-4)*: A GLP-compliant micronucleus test conducted according to OECD Guideline 474 was performed with CFW 1 mice (7/sex/group) administered single gavage doses of sulfuric acid, mono-C16-18-alkyl esters, sodium salts (55% purity) in water at 400, 2,000, or 4,000 mg/kg. The animals were sacrificed after 24 hours (all dose groups) or 48 or 72 hours (4,000 mg/kg only), and bone marrow samples were isolated for the micronuclei assessment. Treatment did not increase the frequency of micronuclei. The authors indicated the vehicle and positive (not identified) controls were valid (Klimisch Score 2, reliable with restrictions).
  - *In vivo: Sulfuric acid, mono-C12-15-alkyl esters, sodium salts (CAS #68890-70-0)*: A non-GLP-compliant chromosome aberration test conducted in a manner similar to OECD Guideline 475 as performed with rats (6/sex/group strain not specified) provided feed containing sulfuric acid, mono-C12-15-alkyl esters, sodium salts (~30% active ingredient) in water at 1.13% for 90 days. At the end of the exposure period, the animals were sacrificed and bone marrow samples were isolated for the chromosome aberration assessment. Treatment did not increase the frequency of chromosome aberrations. The authors indicated that the vehicle and positive (not identified) controls were valid (Klimisch Score 2, reliable with restrictions).

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Low for reproductive toxicity based on lack of treatment related effects on reproductive performance and fertility in a two-generation study of rats exposed to the surrogate mixture of C14:C16:C18 blend (1:1:1:) α-olefin sulfonate, magnesium salt. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is low as no details regarding the specific reproductive/fertility endpoints examined were provided for the surrogate study.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2009, ECHA 2021b
  - *Surrogate: Sodium lauryl sulfate (CAS #151-21-3):* A male fertility study was performed with male Swiss mice (10/group) provided diets containing sodium lauryl sulfate (purity not specified) at 1% for 2 weeks or 0.1% for 6 weeks. Treatment did not produce impairment of epididymal spermatozoa (specific endpoints were not identified) but the animals in the high dose group exhibited significant reductions in average body weight. The REACH and SIDS dossier authors report a reproductive toxicity NOAEL of 1,000 mg/kg/day for this study (Klimisch Score 4, not assignable).
- OECD 2009
  - "No fertility studies were performed with alkyl sulfates."
  - *Surrogate: Mixture of C14:C16:C18 blend (1:1:1:) α-olefin sulfonate, magnesium salt (CAS #N/A):* A two-generation reproductive toxicity study was performed with male and female CD rats (12 males and 24 females/group) provided diets containing mixture of C14:C16:C18 blend (1:1:1:) α-olefin sulfonate, magnesium salt (94.88-95.54% active ingredient) at 0, 1,250, 2,500, or 5,000 ppm for 13 weeks prior to mating, during gestation, and through lactation. The initial parental generation (F0) were mated to generate two successive litters (F1A and F1B). The animals of the F1B litter were reared and mated to produce the F2A and F2B litters. The F2B animals were dosed for 13 weeks and subjected to histopathological evaluation. Based on food intake, the authors report the ingested doses as 0, 63-248, 127-492, and 261-1,040 mg/kg/day across the three generations for the 1,250, 2,500, and 5,000 ppm groups, respectively. Treatment did not adversely affect general health, food consumption or utilization, water intake, body weight gain, reproductive performance, fertility, or gross pathological or histopathological findings. ToxServices notes that the specific reproductive performance and fertility endpoints were not identified, including whether sperm parameters and estrous cyclicity were examined.

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Low for developmental toxicity based on the lack of direct developmental toxicity identified in prenatal animals tests of sodium lauryl sulfate. The adverse effects identified in animal studies are considered secondary to maternal toxicity by OECD. 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 measured data on strong surrogates.

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

- ECHA 2021a
    - *Surrogate: Sulfuric acid, mono-C12-14-alkyl esters, sodium salts (CAS #85586-07-8)*: A non-GLP-compliant prenatal developmental toxicity test conducted in a manner similar to OECD Guideline 414 (partially natural parturition) was performed with pregnant female Wistar rats (20/group, 15 for dissection, 5 for natural parturition) administered gavage doses of sulfuric acid, mono-C12-14-alkyl esters, sodium salts (as Alfol 12-14 sulphate, 100% purity) in water at 0, 63, 125, 250, or 500 mg/kg/day on gestation days 6-15. The animals were sacrificed on gestation day 21. Maternal examinations included clinical signs of toxicity, body weight, food consumption, ovaries, and uterine content. Fetal examinations included litter size, weight, survival, and incidence of external, visceral, and skeletal malformations. Maternal toxicity was evident in the high dose group as reduced food intake and body weight gain and an increased incidence of severe diarrhea. One high dose dam died and two were killed for humane reasons prior to the scheduled sacrifice. Surviving dams in the high dose group exhibited an increased number of intra-uterine fetal deaths and reduced live fetal body weights. These fetuses exhibited delayed ossification and an increased incidence of shortened thoracic ribs and supernumerary cervical ribs. Treatment at 500 mg/kg/day did not increase the incidence of external or visceral malformations. Treatment at lower doses did not negatively affect the number of live fetuses, fetal body weight or crown-rump distance, or the incidence of external, visceral, or skeletal malformations. Treatment did not produce adverse effects on pups born via natural parturition and reared through weaning at 21 days of age. The REACH dossier authors concluded that the developmental deficits and decreased fetal survival at 500 mg/kg/day was secondary to maternal toxicity in this dose group; therefore, they identified maternal toxicity and developmental toxicity NOELs of 250 mg/kg/day and LOELs of 500 mg/kg/day (Klimisch Score 2, reliable with restrictions).
    - *Surrogate: Sodium lauryl sulfate / sodium dodecyl sulfate (CAS #151-21-3)*: A non-GLP-compliant prenatal developmental toxicity test conducted in a manner similar to OECD Guideline 414 (intervals in dose range, lack of details on test substance) was performed with pregnant female CD rats (20/group) administered gavage doses of sodium lauryl sulfate (purity not specified) at 0, 0.2, 2, 300, or 600 mg/kg/day on gestation days 6-15. The animals were sacrificed on gestation day 20. The maternal examinations included body weight, food consumption, ovaries, and uterine content. Fetal examinations included the incidence of visceral and skeletal malformations. Treatment produced unspecified maternal toxic effects in the high dose group, but no evidence of embryotoxicity or teratogenicity was detected at up to the highest dose tested. No additional details were provided. The REACH dossier authors identified a maternal toxicity NOAEL/LOAEL of 300/600 mg/kg/day and a developmental toxicity NOAEL of 600 mg/kg/day, the highest dose tested (Klimisch Score 2, reliable with restrictions).
    - *Surrogate: Sodium lauryl sulfate / sodium dodecyl sulfate (CAS #151-21-3)*: A non-GLP-compliant prenatal developmental toxicity test conducted in a manner similar to OECD Guideline 414 (intervals in dose range and lack of details on test substance) was performed with pregnant female New Zealand White rabbits (13/group) administered gavage doses of sodium lauryl sulfate (purity not specified) in water at 0, 0.2, 2, 300, or 600 mg/kg/day on gestation days 6-18. The animals were sacrificed on gestation day 29. The maternal examinations included body weight, food consumption, ovaries, and uterine content. Fetal examinations included the incidence of visceral and skeletal malformations. Treatment produced unspecified maternal toxic effects in the high dose group, but no evidence of embryotoxicity or teratogenicity was detected at up to the highest dose tested. The REACH

dossier authors identified a maternal toxicity NOAEL/LOAEL of 300/600 mg/kg/day and a developmental toxicity NOAEL of 600 mg/kg/day, the highest dose tested (Klimisch Score 2, reliable with restrictions).

- *Surrogate: Sodium lauryl sulfate / sodium dodecyl sulfate (CAS #151-21-3)*: A non-GLP-compliant prenatal developmental toxicity test was performed with pregnant female Wistar rats (15/group, 10 for dissection and 5 for natural parturition) administered gavage doses of sodium lauryl sulfate (purity not specified) at 0, 63, 125, 250, or 500 mg/kg/day on gestation days 6-15. The animals were sacrificed on gestation day 21 or allowed to give birth and wean the pups up to postnatal day 21. Maternal evaluations included body weight, food consumption, and uterine content (gravid uterus weight, uterine tissue weight, intrauterine mortality, and mean response per pregnancy). Fetal/pup examinations included fetal/pup body weights, crown to rump distance, placental weight, and incidence of external, visceral, and skeletal malformations. All dams in the high dose group exhibited diarrhea. As the course of treatment continued, gavage dosing became progressively more difficult, suggesting a dryness of the gastrointestinal tract, and the animals exhibited more aggressive behavior. In the high dose group, four dams died and one was killed in moribund condition between the 4th and 8th doses. All of the decedent animals exhibited irritation of the gastrointestinal tract and diffuse hemorrhaging of the stomach, and three animals exhibited lung congestion. A high dose dam exhibited a terminated pregnancy after the 9th dose. Treatment statistically significantly reduced maternal body weight gain and food consumption in the high dose group, but did not increase pre- or post-implantation loss. In the high dose group, treatment decreased the mean placental weight for male and female fetuses combined or considered separately ($p = 0.05$). Treatment did not affect the incidence of gross variants/anomalies or skeletal malformations. Three fetuses from separate litters in the high dose group exhibited malformations, which included protruding tongue, gross edema and shortening of the pubic bone; unossified metatarsus and claw in left hind foot; and agenesis of eyelids and cleft palate. Malformations were also identified in one live fetus in the 250 mg/kg/day group, characterized as reduced ossification of the 6th lumbar arch and scoliosis and hermi-centric lumbar centra with asymmetry, and one fetus in the 63 mg/kg/day group, characterized as unossified and dumbbell-shaped thoracic centrae associated with branched ribs. Treatment did not affect postnatal mortality or the incidence of skeletal defects in pups on postnatal say 21. The REACH dossier authors identified a maternal toxicity NOAEL/LOAEL of 250/500 mg/kg/day based on changes to body weight gain and food consumption and a teratogenicity NOAEL of 500 mg/kg/day, the highest dose tested (Klimisch Score 2, reliable with restrictions).
    - ToxServices notes that the malformations observed in three fetuses at the high dose, one fetus at 250 mg/kg, and one fetus at 63 mg/kg are not likely to be treatment-related, due to lack of dose response and the low incidence of occurrence.
- *Surrogate: Sulfuric acid, mono-C16-18-alkyl esters, sodium salts (CAS #68955-20-4)*: A non-GLP-compliant prenatal developmental toxicity test was performed with pregnant female Wistar rats (15/group, 10 for dissection and 5 for natural parturition) administered gavage doses of sulfuric acid, mono-C16-18-alkyl esters, sodium salts (as Alfol 16-18 sulphate, purity not specified) at 0, 112, 225, 450, or 675 mg/kg/day on gestation days 6-15. The animals were sacrificed on gestation day 21 or allowed to give birth and wean the pups up to postnatal day 21. Maternal evaluations included clinical signs of toxicity, food consumption, body weight, ovaries, and uterine content. Treatment increased the incidence of diarrhea in the high dose group, and statistically significantly reduced mean maternal body weight gains on gestation days 6-10 for the 675 mg/kg/day group and on gestation days 10-15 for the 450 mg/kg/day group. No statistically significant differences in food

consumption were identified between the control and treatment groups. Dams in the high dose group had a statistically significantly lower mean number of live fetuses per pregnancy than the concurrent control group. Treatment produced a statistically significantly decreased mean placental weight for male fetuses in the 450 mg/kg/day group. The incidence of macroscopically-observed hemorrhage under the capsule of the kidney was 4.95%, 3.73%, and 3.66% in the 112, 225, and 450 mg/kg groups, respectively (not clear if greater than the control incidence). Treatment increased the incidence of vertebral and head variations/anomalies in the 112 mg/kg/day group. Following natural parturition, 5/6 pups in a single litter born from a high dose dam were cannibalized during postnatal days 1-3. Additionally, two pups from a single litter born from a dam administered 450 mg/kg/day were cannibalized. No additional details were provided. The REACH dossier authors identified a maternal toxicity NOAEL/LOAEL of 225/450 mg/kg/day based on reduced body weight gains and a embryotoxicity NOAEL of 675 mg/kg/day, the highest dose tested (Klimisch Score 2, reliable with restrictions).

  - ToxServices notes that the decreased mean placental weight for male fetuses at 450 mg/kg, increased vertebral and head variations/anomalies at 112 mg/kg, and cannibalism of pups from a single litter each at 450 and 675 mg/kg are not likely treatment-related due to lack of dose response.

- In summary, while some studies identified increased incidences in skeletal and/or visceral variations or malformations following *in utero* exposure to the surrogate alkyl sulfates, these effects appear to be secondary to maternal toxicity, characterized as statistically significantly decreased body weight gains and/or food consumption and clinical signs of toxicity including diarrhea. The increase in fetal skeletal variations may reflect delayed development due to nutritional deficits following treatment (OECD 2009). Therefore, ToxServices assigned a Low score for this endpoint based on the lack of evidence for direct developmental toxicity by the surrogate alkyl sulfates.

Endocrine Activity (E) Score (H, M, or L): DG
Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Data Gap for endocrine activity based on insufficient data identified for this endpoint.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- U.S. EPA 2021
  - *Surrogate: Sodium lauryl sulfate / sodium dodecyl sulfate (CAS #151-21-3)*: The surrogate sodium lauryl sulfate was active in 2/21 estrogen receptor (ER) assays, 2/15 androgen receptor (AR) assays, 0/2 steroidogenesis assays, and 9/17 thyroid receptor assays performed as part of the U.S. EPA's Endocrine Disruptor Screening Program (EDSP) in the 21st Century (Appendix D).
  - *Surrogate: Sodium lauryl sulfate / sodium dodecyl sulfate (CAS #151-21-3)*: The surrogate sodium lauryl sulfate was predicted to be inactive for estrogen receptor agonism but to have very weak antagonism and binding using the CERAPP Potency Level (Consensus and/or From literature) models. It was predicted to be inactive for androgen receptor agonism, antagonism, and binding using the COMPARA (Consensus) model in ToxCast (Appendix E).
- VEGA 2020 (Note: ToxServices could not model the full structure of sulfuric acid, mono-C12-18-alkyl esters, sodium salts in VEGA as it does not evaluate ionic substances. Therefore, ToxServices input the structure for lauryl (C12) sulfate (CAS #151-41-7), the shortest and likely most

bioavailable alkyl chain in the target chemical, as the sodium moiety is not expected to contribute endocrine activity.)
    - Lauryl sulfate was predicted to be active in the Estrogen Receptor Relative Binding Affinity model (IRFMN) with low reliability [Global applicability domain (AD) Index = 0] (Appendix F).
    - Lauryl sulfate was predicted to be non-active in the Estrogen Receptor-mediated effect (IRFMN/CERAPP) 1.0.0 model with low reliability (Global AD Index = 0) (Appendix F).
    - Lauryl sulfate was predicted to be non-active in the Androgen Receptor-mediated effect (IRFMN/COMPARA) 1.0.0 model with strong reliability (Global AD Index = 0.991, similarity index = 0.982, accuracy index = 1, concordance index = 1) (Appendix F).
    - Lauryl sulfate was predicted to be inactive in the Thyroid Receptor Alpha effect (NRMEA) 1.0.0 model with strong reliability (Global AD Index = 0.982, similarity index = 0.965, accuracy index = 1, concordance index = 1) (Appendix F).
    - Lauryl sulfate was predicted to be inactive in the Thyroid Receptor Beta effect (NRMEA) 1.0.0 model with strong reliability (Global AD Index = 0.982, similarity index = 0.965, accuracy index = 1, concordance index = 1) (Appendix F).
    - Lauryl sulfate was predicted to be inactive in the Aromatase activity (IRFMN) 1.0.0 model with moderate reliability (Global AD Index = 0.775, similarity index = 0.831, accuracy index = 1, concordance index = 1) (Appendix F).
- DTU 2021
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts, its predicted metabolites from *in vivo* rat metabolism simulator, and predicted metabolites from the rat liver S9 metabolism simulator, contain no structural alerts for estrogen receptor binding (Appendix G).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts was predicted to be negative and in domain by the Leadscope model for estrogen receptor activation, CERAPP data (*in vitro*) (Appendix G).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts was predicted to be negative and in domain by the Leadscope model for androgen receptor binding, CoMPARA data (*in vitro*), androgen receptor inhibition, CoMPARA data (*in vitro*), and androgen receptor activation, CoMPARA data (*in vitro*) (Appendix G).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts was predicted to be negative and in domain by thyroperoxidase (TPO) inhibition QSAR1 (Rat *in vitro*) and QSAR2 (Rat *in vitro*) models (Appendix G).
- Based on the weight of evidence, ToxServices assigned a Data Gap for endocrine activity. The available *in vitro* high through-put results for the surrogate sodium lauryl sulfate and modeling results indicate that sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is not likely to interact with ER, AR, or thyroid receptors or affect steroidogenesis. However, no *in vivo* data are available to determine its effects on circulating estrogen, androgen, and thyroid hormone levels. Therefore, ToxServices assigned a Data Gap for this endpoint.

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Low for acute toxicity based on an oral LD_{50} of 4,010 mg/kg and a dermal LD_{50} > 2,000 mg/kg for the surrogate sodium octyl sulfate. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD_{50}s are greater than 2,000 mg/kg (CPA 2018b). The confidence in the score is high as it is based on reliable measured data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - GHS - New Zealand - 6.1D (oral) - Acutely toxic (GHS Category 4).
      - Based on the EU Risk Phrase R22 (equivalent to GHS Category 4, H302) (CCID 2021).
- ECHA 2021a
  - *Oral*: LD_{50} (Cox CD rats) = 4,010 mg/kg (similar to OECD Guideline 401) (Klimisch Score 2, reliable with restrictions).
  - *Oral*: LD_{50} (Wistar rats) > 2,000 mg test material/kg (GLP-compliant, EU Method B.1) (Klimisch Score 1, reliable without restriction).
    - Based on a purity of 30%, the equivalent dose for sulfuric acid, mono-C12-18-alkyl esters, sodium salts is > 600 mg/kg.
  - *Oral*: LD_{50} (Sprague Dawley rats) > 500 mg/kg (GLP status not specified, similar to OECD Guideline 401) (Klimisch Score 2, reliable with restrictions).
  - *Oral*: LD_{50} (rat) > 5,000 mg/kg (non-GLP-compliant, similar to OECD Guideline 401) (Klimisch Score 4, not assignable).
  - *Dermal: Surrogate: Sodium octyl sulfate (CAS #142-31-4)*: LD_{50} (Wistar rats) > 2,000 mg/kg (GLP-compliant, OECD Guideline 402) (Klimisch Score 2, reliable with restrictions).
  - *Dermal*: *Surrogate: Sulfuric acid, mono-C12-13-alkyl esters, potassium salts (CAS #91783-22-1)*: LD_{50} (New Zealand White rabbits) > 2,000 mg test material/kg (pre-GLP, similar to OECD Guideline 402) (Klimisch Score 2, reliable with restrictions).
    - Based on a purity of 25%, this is equivalent to > 500 mg active ingredient/kg.
  - *Dermal*: *Surrogate: Sulfuric acid, mono-C10-16-alkyl esters, magnesium salts (CAS #68081-97-0)*: LD_{50} (New Zealand White rabbits) > 2,000 mg test material/kg (pre-GLP, similar to OECD Guideline 402) (Klimisch Score 2, reliable with restrictions).
    - Based on a purity of 23.5%, the LD_{50} is equivalent to > 500 mg active substance/kg.
  - *Dermal*: *Surrogate: Sulfuric acid, mono-C10-16-alkyl esters, ammonium salts (CAS #68081-96-9)*: LD_{50} (New Zealand White rabbits) > 2,000 mg test material/kg (pre-GLP, similar to OECD Guideline 402) (Klimisch Score 2, reliable with restrictions).
    - Based on a purity of 25.1%, the LD_{50} is equivalent to > 500 mg active substance/kg.

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Moderate for systemic toxicity (single dose) based on ToxServices classifying them as Category 3 specific target organ toxicants following single exposures for respiratory irritation under GHS criteria. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (single dose) when they are classified as GHS Category 3 specific target organ toxicants following single exposures for respiratory irritation (CPA 2018b). The confidence in the score is low as evidence of respiratory irritation were identified only in one acute oral toxicity test.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
  - *Oral*: In the acute oral toxicity test similar to OECD Guideline 401 that identified an oral LD_{50} of 4,010 mg/kg in Cox CD rats, clinical signs of toxicity included slightly to moderately decreased respiratory rate and motor activity, diarrhea, blanching, and abdominal griping at ≥ 2,500 mg/kg; slight hemorrhagic rhinitis (inflammation and swelling of the nasal mucous membrane) at ≥ 3,500 mg/kg; and slightly decreased pupillary responses and corneal reflex at 6,850 mg/kg. No body weight data were provided. The surviving animals did not exhibit treatment-related changes to necropsy findings (Klimisch Score 2, reliable with restrictions).
  - *Oral*: In the GLP-compliant, EU Method B.1 acute oral toxicity test that identified an oral LD_{50} > 2,000 mg test substance/kg (> 600 mg active substance/kg; the only dose tested) in Wistar rats, treatment did not affect mortality, clinical signs of toxicity, body weight, or gross pathological findings (Klimisch Score 1, reliable without restriction).
  - *Oral*: In the acute oral toxicity test similar to OECD Guideline 401 that identified an oral LD_{50} > 500 mg/kg in Sprague Dawley rats, treatment did not produce mortality or clinical signs of toxicity. No details on gross pathological findings were provided (Klimisch Score 2, reliable with restrictions).
  - *Oral*: In the acute oral toxicity test similar to OECD Guideline 401 that identified an oral LD_{50} > 5,000 mg/kg in an unidentified strain of rats, no details regarding clinical signs of toxicity, body weight, or gross pathological findings were provided (Klimisch Score 4, not assignable).
  - *Dermal: Surrogate: Sodium octyl sulfate (CAS #142-31-4)*: In the GLP-compliant, OECD Guideline 402 acute dermal toxicity test that identified a dermal LD_{50} > 2,000 mg/kg in Wistar rats) > 2,000 mg/kg (GLP-compliant, OECD Guideline 402), treatment did not produce mortality or clinical signs of toxicity. Body weight increases were within the normal range for males throughout the observation period and for females during the second week of the observation period. The authors speculate that the lack of body weight increase for females during the first week was due to the bandage procedure. Treatment did not produce local effects on the skin of the application site or gross pathological changes (Klimisch Score 2, reliable with restrictions).
  - *Dermal*: *Surrogate: Sulfuric acid, mono-C12-13-alkyl esters, potassium salts (CAS #91783-22-1)*: In the pre-GLP acute dermal toxicity test similar to OECD Guideline 402 that identified a dermal LD_{50} > 2,000 mg test material/kg (> 500 mg active ingredient/kg) in New Zealand White rabbits, treatment did not produce mortality or body weight losses. At the application site, treatment produced moderate to severe erythema, edema, and atonia (loss of muscle tone), with all animals exhibiting desquamation (peeling), fissuring (cleavage), eschar, and exfoliation by day 6 of the observation period. Signs of skin irritation were still evident in all six animals at study termination. No details regarding gross pathological findings were provided (Klimisch Score 2, reliable with restrictions).
  - *Dermal*: *Surrogate: Sulfuric acid, mono-C10-16-alkyl esters, magnesium salts (CAS #68081-97-0)*: In the acute dermal toxicity test that identified a dermal LD_{50} > 2,000 mg test material/kg (> 500 mg active substance/kg) in New Zealand White rabbits, treatment did not produce mortality or clinical signs of toxicity aside from effects to the application site skin. Treated animals exhibited severe erythema and eschar formation within 24 hours of dosing, and necrosis developed on days 5-21 of the observation period. By day 21, the necrotic

tissues sloughed away, leaving the skin hyper-pigmented. All but one animal exhibited weight loss during the observation period. No gross pathology data were provided (Klimisch Score 2, reliable with restrictions).

- *Dermal*: *Surrogate: Sulfuric acid, mono-C10-16-alkyl esters, ammonium salts (CAS #68081-96-9)*: In the acute dermal toxicity test that identified a dermal LD_{50} > 2,000 mg test material/kg (> 500 mg active substance/kg) in New Zealand White rabbits, treatment did not produce mortality or clinical signs of toxicity aside from effects at the application site. Treatment animals exhibited severe erythema and slight eschar 24 hours after dosing, with necrosis developing on days 2-14, sloughing of the skin on days 8-14, and hyper-pigmentation of new skin by day 14 of the observation period. One rabbit with intact skin exhibited decreased body weight during the observation period. No gross pathological data were provided (Klimisch Score 2, reliable with restrictions).

- In summary, no evidence of gross pathological changes in systemic organs following single oral or dermal doses of sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate. In the OECD Guideline 401 study performed with Cox CD rats, the treated animals exhibited decreased respiratory rate and hemorrhagic rhinitis. The hemorrhagic rhinitis is likely due to irritation to the nasal epithelium. While the decreased respiratory rate could be due to decreased activity and discomfort following dosing with an irritating substance, it may also be a reflection of respiratory irritation. While ToxServices identified no acute inhalation studies for sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate or related alkyl sulfate salts, these chemicals are ocular irritants (see the eye irritation/corrosivity section below), indicating that they are irritating to mucous membranes. Therefore, ToxServices conservatively classified sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate as a Category 3 specific target organ toxicant following single exposures for respiratory irritation under GHS criteria (UN 2019).

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Low for systemic toxicity (repeated dose) based on ToxServices not classifying them as specific target organ toxicants following repeated exposures under GHS criteria. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when they are not classified as GHS specific target organ toxicants following repeated exposures (CPA 2018b). The confidence in the score is high as it is based on reliable measured data from subchronic and chronic duration studies.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
  - *Oral*: *Surrogate: Sulfuric acid, mono-C12-15-alkyl esters, sodium salts (CAS #68890-70-0)*: A non-GLP-compliant subchronic repeated dose toxicity study conducted in a manner similar to OECD Guideline 408 was performed with Colworth Wistar-derived rats (20/sex in control group, 10/sex in treatment groups) provided diets containing the surrogate sulfuric acid, mono-C12-15-alkyl esters, sodium salts (30% active ingredient) at 0.07, 0.14, 0.28, 0.56, 1.13, or 2.25% (resulting in equivalent doses of 58, 113, 228, 470, 961, and 1,944 mg/kg/day for males and 66, 131, 261, 506, 1,070 and 2,218 mg/kg/day for females, respectively) for 13 weeks. The animals were evaluated for clinical signs of toxicity, body weight, food and water intake, hematology, clinical chemistry, organ weights, gross

pathology, and histopathology. One male in each of the 0.14% and 1.13% groups were sacrificed during the course of the study due to morbidity the authors reported as arising from lesions occasionally observed in this strain of rat. The authors did not consider these effects to be treatment-related. Treatment significantly reduced body weight gain in high dose females (16% decrease) and in males in the 1.13% group (10% decrease) and high dose group (20% decrease). The effects on body weight correlated with significantly decreased food consumption values in high dose males (9% decrease) and females (6% decrease), and significantly decreased food utilization in high dose males (13% decrease) and females (10% decrease) and in males in the 1.13% group (5% decrease). High dose females also exhibited a 15% decrease in water intake. Treatment did not adversely affect hematology parameters, but treatment-related effects on clinical chemistry parameters included significantly decreased protein, magnesium, and cholesterin levels and increased aspartate aminotransferase (AST, GOP), alanine aminotransferase (ALT, GPT), and alkaline phosphatase (AP) in high dose males; increased AP in high dose females; increased AP in 1.13% treatment group males; increased GPT in 1.13% treatment group females; and increased AP in 0.28% and 0.56% males. Treatment altered organ weights as indicated in the following table.

Organ	**Weight**	**Dietary Concentration (%)**					
		0.07	0.14	0.38	0.56	1.13	2.25
Liver	Relative				↑ m/f	↑ m/f	↑ m/f
	Absolute					↑ f	↑ f
Spleen	Relative						
	Absolute					↓ m	↓ m/f
Kidney	Relative					↑ f	↑ f
	Absolute						↓ m
Brain	Relative					↑ m	↑ m/f
	Absolute						
Testes	Relative					↑ m	↑ m
	Absolute						
Heart	Relative						↑ m
	Absolute					↓ m	↓ m/f

Treatment-related gross pathological changes included changes and color of the intestinal contents in high dose males and females and in males in the 1.13% treatment group, and no abdominal fat in high dose males. Treatment produced histopathological changes in the liver, kidney, alimentary tract, and connective tissue. In the liver, increased incidences of diffuse and periportal hypertrophy, reduced cytoplasmic (glycogenic) vacuolation, reduced hepatic parenchyma cytoplasmic and Kupffer cell hemosiderin content, and decreased hepatic parenchyma cytoplasmic neutral fat in the high dose group. Additionally, the incidence of diffuse hypertrophy increased in females in the 1.13% group and the incidence of periportal hypertrophy increased in males and females in this dose group. Females in the 0.28% group also exhibited an increased incidence of periportal hypertrophy. Decreased cytoplasmic neutral fat, hemosiderin content, and cytoplasmic (glycogenic) vacuolation were also detected in males and/or females in the 0.56-2.25% groups. The authors considered the histopathological changes in the liver to be adaptive responses to the treatment, rather than adverse. In the kidney, high dose females exhibited decreased incidences and/or severity of nephrocalcinosis, cortical interstitial fibrosis, small foci of cortical tubular atrophy, and focal

lymphocytic infiltration, which are commonly identified in females of this rat strain. High dose animals exhibited lymphatic dilation of the small intestine, attributable to an increased extent of dilation of individual vessels and an increase in the number of visible lymphatic channels, and an increased incidence of protozoan parasite colonization. Treatment also decreased the quantity of stromal lipid in the pancreas and parotid salivary glands. The authors identified a NOAEL of 0.56% (equivalent to 470-506 mg/kg/day) based on increased testicular weights in males at 1.13% (961 mg/kg/day) (Klimisch Score 2, reliable with restrictions).

- *Oral: Surrogate: Sodium lauryl sulfate / sodium dodecyl sulfate (CAS #151-21-3):* A subchronic repeated dose toxicity study (GLP status not specified) conducted in a manner similar to OECD Guideline 408 was performed with male and female rats (strain and number not specified) provided diets containing sodium lauryl sulfate (86% active ingredient) at 0, 40, 200, 1,000, or 5,000 ppm (contributing doses equivalent to 0, 3, 17, 86, and 430 mg/kg/day, respectively) for 90 days. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, urinalysis, clinical signs of toxicity, hematology, gross pathology, and histopathology. The only treatment-related effect identified was increased liver weights in high dose female rats, which the authors considered to be an adaptive effect. The authors identified a NOAEL of 430 mg/kg/day, the highest dose tested (Klimisch Score 2, reliable with restrictions).
- *Oral: Surrogate: Sodium lauryl sulfate / sodium dodecyl sulfate (CAS #151-21-3):* A non-GLP-compliant subchronic repeated dose toxicity study conducted in a manner similar to OECD Guideline 408 was performed with Wistar rats (10/sex/treatment group, 20/sex in the control group) provided diets containing sodium lauryl sulfate (99% active ingredient) at 0, 0.07%, 0.14%, 0.28%, 0.56%, 1.13%, or 2.25% (contributing doses equivalent to 0, 58, 116, 230, 460, 920, or 1,840 mg/kg/day, respectively) continuously for 13 weeks. Treatment only produced adaptive changes in the liver, characterized as increased liver weights and hepatic hypertrophy, and the REACH dossier authors identified a NOAEL/LOAEL of 460/920 mg/kg/day. No additional details were provided (Klimisch Score 2, reliable with restrictions).
- *Oral: Surrogate: Sulfuric acid, mono-C16-18-alkyl esters, sodium salts (CAS #68955-20-4)*: A non-GLP-compliant subchronic repeated dose toxicity study conducted in a manner similar to OECD Guideline 408 was performed with Wistar rats (10/sex/treatment group, 20/sex in the control group) provided diets containing sulfuric acid, mono-C16-18-alkyl esters, sodium salts (31.5% active ingredient) at 0%, 0.07%, 0.14%, 0.28%, 0.56%, 1.13%, or 2.25% (contributing doses equivalent to 0, 61, 123, 230, 482, 970, and 2,067 mg/kg/day, respectively) continuously for 13 weeks. Treatment only produced adaptive changes in the liver, characterized as increased liver weights and hepatic hypertrophy, and the REACH dossier authors identified a NOAEL/LOAEL of 482/970 mg/kg/day. No additional details were provided (Klimisch Score 2, reliable with restrictions).
- *Oral: Surrogate: Sulfuric acid, mono-C10-16-alkyl esters, sodium salts (CAS #68585-47-7):* A pre-GLP subchronic repeated dose toxicity study conducted in a manner similar to OECD Guideline 408 was performed with Sprague-Dawley (Charles River CD) rats (20/sex/group) provided diets containing sulfuric acid, mono-C10-16-alkyl esters, sodium salts (29.6% active ingredient) at 0%, 0.25%, 0.%, or 1% (contributing doses equivalent to 0, 55.5, 112.48, and 201.28 mg/kg/day for males and 0, 59.94, 122.84, and 254.56 mg/kg/day for females, respectively) continuously for 90 days. The animals were evaluated for clinical signs of toxicity, body weight, food consumption and efficiency, ophthalmology, hematology, clinical chemistry, urinalysis, gross pathology, and histopathology. Treatment did not adversely affect these parameters and the REACH dossier authors identified a

NOAEL of 1% (equivalent to 201.28-254.56 mg/kg/day), the highest dose tested (Klimisch Score 1, reliable without restriction).

- *Oral*: *Surrogate: Sulfuric acid, mono-C12-15-alkyl esters, sodium salts (CAS #68890-70-0)*: A non-GLP-compliant combined chronic toxicity/carcinogenicity test conducted in a manner similar to OECD Guideline 453 was performed with Colworth Wistar rats (45/sex/group) provided diets containing the surrogate sulfuric acid, mono-C12-15-alkyl esters, sodium salts (30.1% purity) at 0.015, 0.15, or 1.5% (contributing doses equivalent to 11, 113, and 1,125 mg/kg/day, respectively) for two years. The animals were evaluated for clinical signs of toxicity, body weight, food and water consumption, hematology, clinical chemistry, gross pathology, and histopathology. Treatment did not adversely affect survival, but high dose animals exhibited decreased body weight gain, food consumption, and water consumption relative to the control group. High dose females also exhibited a decreased total white blood cell count. High dose males exhibited increased serum ALT and AP activities and increased urea levels, while high dose females exhibited decreased lactate dehydrogenase and hydroxybutyrate dehydrogenase activities. The authors attributed the increased AP activity to hepatic parenchymal hypertrophy and the increased ALT activity to multifocal sub-lobular hepatic necrosis. High dose males exhibited reduced relative weights for the heart, kidneys, spleen, and adrenal glands and increased absolute and relative testes weights, while high dose males and females exhibited increased absolute and relative liver weights. Treatment produced an increased incidence of diffuse hepatic enlargement in the high dose group. This gross pathological finding correlated with increased incidences and severity of hepatic parenchymal hypertrophy, focal coagulative and/or hemorrhagic necrosis and pigmented lipid granuloma in the liver of high dose animals. The authors considered the pathological changes to the liver to be representative of adaptive changes and/or changes typically identified in aging rats of this strain. In high dose females, treatment reduced the severity of splenic extramedullary erythropoiesis and the incidence of splenic myelopoiesis and stem cell hyperplasia but increased the severity of red pulp hemosiderin deposition. High dose rats exhibited decreased incidences and/or severity of chronic nephropathy and pelvic nephrocalcinosis in the kidney and/or arterial medial hypertrophy in the heart. The authors identified a NOAEL/LOAEL of 113/1,125 mg/kg/day based on the adaptive changes to the liver and increased severity of red pulp hemosiderin deposition in the spleen (Klimisch Score 2, reliable with restrictions).
- *Oral: Surrogate: Sulfuric acid, mono-C13-15-alkyl esters, sodium salts (CAS #86014-79-1):* A non-GLP-compliant subchronic repeated dose toxicity test conducted in a manner similar to OECD Guideline 408 was performed with Wistar rats (20/sex in control group, 10/sex in treatment groups) provided diets containing the surrogate sulfuric acid, mono-C13-15-alkyl esters, sodium salts (30.5% purity) at 0, 0.07, 0.14, 0.28, 0.56, 1.13, or 2.25% (resulting in equivalent doses of 0, 64, 134, 253, 512, 1,007, and 2,096 mg/kg/day, respectively) for 13 weeks. Treatment only produced adaptive changes in the liver, characterized as increased liver weights and hepatic hypertrophy, and the REACH dossier authors identified a NOAEL/LOAEL of 512/1,007 mg/kg/day. No additional details were provided (Klimisch Score 2, reliable with restrictions).
- *Dermal: Surrogate: Sulfuric acid, mono-C12-15-alkyl esters, sodium salts (CAS #68890-70-0):* A non-GLP-compliant subchronic dermal repeated dose toxicity test conducted prior to implementation of but in a manner similar to OECD Guideline 411 (applications only twice per week, deficiencies in hematology and clinical chemistry data) was performed with C57BL mice (10/sex/group) administered topical applications of 0.2 mL of the surrogate sulfuric acid, mono-C12-15-alkyl esters, sodium salts (30.1% purity) in water at nominal concentrations of 0, 5, 10, 12.5, or 15% (calculated by the REACH dossier authors as

equivalent to doses of 0, 200, 400, 500, and 600 mg/kg/day, respectively, assuming 20 g/mouse and 5 days/week exposure frequency) twice weekly for 13 weeks. The type of coverage was not specified. The animals were evaluated for body weight, water intake, hematology (white cell count, packed cell volume, hemoglobin level, and mean corpuscular hemoglobin concentration), and organ weights and histopathology (liver, spleen, kidney, brain, heart, and testes). One animal in the 12.5% group died after one week of treatment due to anorexia and dehydration. Water intake increased for all animals provided ≥ 10% test substance. High dose males exhibited decreased hemoglobin levels and increased white blood cell counts. High dose females exhibited increased absolute and relative heart weights, while females in the 12.5% group and males and females in the 15% group exhibited increased relative liver weights. High dose males and females also exhibited increased absolute an relative kidney weights, respectively. Gross pathological and histopathological changes were limited to the skin of the application site and included cytotoxic effects in the epidermis at 12.5% and 15%, exudate adherent to skin (4/20 animals) in the high dose group, loss of hair color lateral and ventral to application site in all dose groups, and dose-related ulceration of the epidermis (4/20 animals) with inflammatory exudate (11/20 animals) in the two highest dose groups. The decedent animal exhibited extensive ulceration and necrosis of the epidermis. The REACH dossier authors identified a NOAEL/LOAEL of 400/500 mg/kg/day based on effects on organ weights, hematology parameters, and gross pathological changes to the skin in the two highest dose groups (Klimisch Score 2, reliable with restrictions).

  - Additional repeated oral dose toxicity studies are presented in the REACH dossier for sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate but were assigned Klimisch Scores of 3 (not reliable); therefore, ToxServices did not include the results of these studies in the present assessment.

- In summary, the liver is the target organ following repeated oral dosing of related alkyl sulfates based on altered serum enzymes, increased liver weights, and histopathological changes. The NOAELs for the subchronic repeated dose toxicity studies were greater than the GHS oral threshold of 100 mg/kg/day (UN 2019). Therefore, ToxServices assigned a Low score for this endpoint.

Neurotoxicity (single dose, N-single) (Group II) Score (vH, H, M, or L): *M*
Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Moderate for neurotoxicity (single dose) based on ToxServices classifying it as a Category 3 specific target organ toxicant following single exposures for narcotic effects under GHS criteria. GreenScreen® criteria classify chemicals as a Moderate hazard for neurotoxicity (single dose) when they are classified as GHS Category 3 specific target organ toxicant following single exposures for narcotic effects (CPA 2018b). The confidence in the score is low as it is based on effects identified only in one study and it is not clear if the decreased motor activity was neurological in nature or manifestation of discomfort following exposure to an irritating 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 2021a
  - *Oral*: In the acute oral toxicity test similar to OECD Guideline 401 that identified an oral LD_{50} of 4,010 mg/kg in Cox CD rats, clinical signs of toxicity included slightly to moderately decreased motor activity at ≥ 2,500 mg/kg, and slightly decreased pupillary responses and corneal reflex at 6,850 mg/kg (Klimisch Score 2, reliable with restrictions).

- In summary, the results of one acute oral toxicity test in rats indicated reduced motor activity and decreased pupillary responses and corneal reflex following single doses of sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate. As specific neurotoxicity tests were not included in this test, and the treated animal's decreased activity could be a manifestation of discomfort following exposure to an irritating substance, it is not clear if the decreased motor activity was neurological in nature. The decreased pupillary responses and corneal reflex likely have a neurotoxicological basis but the dose at which this effect was observed (6,850 mg/kg) is significantly higher than the LD_{50} (4,010 mg/kg) identified for this study. Effects occurring at or above lethal doses should not be used as the basis to classify chemicals for this endpoint. Therefore, ToxServices did not consider neurological effects at the oral dose of 6,850 mg/kg to be appropriate for classification. As it is not clear whether the etiology of the decreased motor activity detected at 2,500 mg/kg, which is less than the LD_{50} of 4,010 mg/kg, is neurological or is a manifestation of discomfort following exposure to an irritating substance, ToxServices conservatively classified sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate as a Category 3 specific target organ toxicant following single exposure for narcotic effects under GHS criteria (UN 2019).

Neurotoxicity (repeated dose, N-repeated) (Group II*) Score (H, M, or L): DG
Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Data Gap for neurotoxicity (repeated dose) based on the lack of data identified for this endpoint.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ToxServices identified no data for this endpoint.

Skin Sensitization (SnS) (Group II*) Score (H, M, or L): L
Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Low for skin sensitization based on negative results in a Buehler test and two guinea pig maximization tests. 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 high as it is based on reliable measured data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
  - A GLP-compliant Buehler test conducted according to OECD Guideline 406 was performed with female Dunkin-Hartley guinea pigs (20 in treatment group, 10 controls) administered dermal doses of sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (100% active ingredient). The induction and challenge doses were applied as 12.5% and 6.25% solutions, respectively, in water under occlusive dressing. One animal in the treatment group died accidentally on day 29. After 24 and 48 hours, treatment produced positive dermal reactions in 4/20 (20%) and 2/19 (10.5%) animals. The negative control animals exhibited 2/10 (20%) and 0/10 positive reactions after 24 and 48 hours, respectively. Since the treatment produced the same incidence of positive dermal reactions as the negative control group at 24 hours, the authors concluded that the test substance was not sensitizing to the skin under the tested conditions (Klimisch Score 1, reliable without restriction).

- A guinea pig maximization test conducted in a manner similar to EU Method B.6 (GLP status not specified) was performed with guinea pigs (strain not specified, 20 in treatment group, 10 controls) administered dermal doses of sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (as FAS C12/C18, 25% active ingredient). No details were provided for the induction doses. The animals were challenged with 12.5% solutions of the test substance. At 24 and 48 hours, the treatment produced 2/20 (10%) and 0/20 positive dermal reactions, respectively, compared to 0/10 reactions for the negative control group at both time points. The authors concluded that the test substance was not sensitizing to the skin under the tested conditions (Klimisch Score 2, reliable with restrictions).
- A guinea pig maximization test conducted in a manner similar to OECD Guideline 406 (GLP status not specified) was performed with guinea pigs (strain not specified, 10 in treatment group, 4 controls) administered dermal doses of sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (purity not specified). No details were provided for the induction doses. The animals were challenged with 50% or 100% solutions of the test substance. At 24 and 48 hours, no positive dermal reactions were identified in the treatment or negative control groups. The authors concluded that the test substance was not sensitizing to the skin under the tested conditions (Klimisch Score 2, reliable with restriction).

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Low for respiratory sensitization based on the lack of dermal sensitization potential according to the ECHA guidance (2017). GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when they are not GHS classified (CPA 2018b). 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 2020a
  - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate does not contain any structural alerts for respiratory sensitization, based on analysis of a representative structure (Appendix H).
- 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 sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate 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 sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate, and as sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate does not contain any structural alerts for respiratory sensitization (OECD 2020a), sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is not expected to be a respiratory sensitizer.

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of High for skin irritation/corrosivity based on ToxServices classifying it as a Category 2 skin irritant under GHS criteria. GreenScreen® criteria classify chemicals as a High hazard for skin irritation/corrosivity when they are classified as GHS Category 2 skin irritants (CPA 2018b). The confidence in the score is high as it is based on reliable measured data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - GHS – Australia - H315 - Causes skin irritation.
      - Based on dermal irritation effects in rabbit studies (AICS 2015).
    - GHS - New Zealand - 6.3A - Irritating to the skin (Cat. 2).
      - Based on the EU Risk Phrase R38 (equivalent to GHS Category 2, H315) (CCID 2021).
- ECHA 2021a
  - A GLP-compliant dermal irritation test conducted according to OECD Guideline 404 was performed with New Zealand White rabbits (3 total) administered topical applications of 0.5 g sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (88.7% active ingredient) without dilution to shaved skin under semi-occlusive dressing for 4 hours. An observation period of 14 days followed the exposure period. At 24, 48, and 72 hours, the mean erythema and edema scores were 3/4 and 2.3/4, respectively. The irritation effects fully resolved by the end of the observation period. The authors concluded that the test substance was irritating to the skin under the tested conditions (Klimisch Score 1, reliable without restriction).
  - A non-GLP-compliant dermal irritation test was performed with mice (strain and number not specified) administered topical applications of 10% sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (35% active ingredient in water) for five days. The type of coverage and vehicle (if used) were not identified. Treatment did not produce dermal irritation in this study (Klimisch Score 2, reliable with restrictions).
  - A non-GLP-compliant dermal irritation test was performed with rabbits (strain and number not specified) administered topical applications of 5% sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (35% active ingredient in water) for four hours. The type of coverage and vehicle (if used) were not identified. Treatment produced slight dermal irritation that was fully reversible (Klimisch Score 2, reliable with restrictions).
  - A 5% solution of sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (purity not specified) was not irritating to the skin of mice (strain and number not specified). No further details were provided (Klimisch Score 2, reliable with restrictions).
  - Additionally studies presented in the REACH dossier were assigned Klimisch Scores of 3 (not reliable) or 4 (not assignable); therefore, ToxServices did not include the results of these studies in the present assessment.
- GHS criteria define skin irritants as chemicals that produce mean scores ≥ 1.5 and < 2.3 (Category 3) or ≥ 2.3 and ≤ 4.0 (Category 2) for erythema and/or edema in at least 2 of 3 animals following readings at 24, 48, and 72 hours (UN 2019). Corrosive materials or those producing irreversible effects to the skin (i.e., visible necrosis) are classified to Category 1. Only the first study summarized above had sufficient documentation and level of detail to compare the results against

the GHS criteria. Since the mean erythema score of 3 falls in the first study summarized above falls within the ≥ 2.3 and ≤ 4.0 range for Category 2, ToxServices classified sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate as a Category 2 skin irritant under GHS criteria. This is in agreement with the classifications from Australia and New Zealand.

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Very High for eye irritation/corrosivity based on ToxServices classifying it as a Category 1 eye irritant under GHS criteria. GreenScreen® criteria classify chemicals as a Very High hazard for eye irritation/corrosivity when they are classified as GHS Category 1 eye irritants (CPA 2018b). The confidence in the score is high as it is based on reliable measured data for strong surrogates.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - GHS – Australia - H318 - Causes serious eye damage.
      - Based on ocular irritation effects in rabbit studies (AICS 2015).
- ECHA 2021a
  - An ocular irritation test conducted in a manner similar to OECD Guideline 405 was performed with New Zealand rabbits (six total) administered ocular instillations of 0.1 mL sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (6% active substance). An observation period of 72 hours followed the instillations. At 24, 48, and 72 hours, the mean corneal opacity score was 0/4, the mean iris score was 0/2, the mean conjunctival score was 0.9/3, and the mean chemosis score was 0.1/4. All of the ocular irritation effects fully resolved within 72 hours. The authors concluded that the test substance was not irritating under the tested conditions.
  - A non-GLP-compliant ocular irritation test was performed with rabbits (strain not specified, five total) administered ocular instillations of 5% sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (35% active ingredient in water). The irritation score (not defined) was 16, 16, 8, 0, and 0 after 2, 6, 24, 48, and 72 hours, respectively. The authors concluded that the test substance was not irritating under the tested conditions.
  - *Surrogate: Sulfuric acid, mono-C12-16-alkyl esters, sodium salts (CAS #73296-89-6)*: A GLP-compliant ocular irritation test conducted according to OECD Guideline 405 was performed with New Zealand White rabbits (3 total) administered ocular instillations of 0.1 mL of sulfuric acid, mono-C12-16-alkyl esters, sodium salts (30% active ingredient) without dilution. An observation period of 21 days followed the instillations. At 24, 48, and 72 hours, the mean corneal opacity score was 1/4, the mean iris score was 0.2/2, the mean conjunctival score was 2.8/3, and the mean chemosis score was 3.6/4. Only the chemosis was fully reversible by the end of the observation period. The authors concluded that the test substance was irritating to the eyes under the tested conditions (Klimisch Score 2, reliable with restrictions).
  - *Surrogate: Sulfuric acid, mono-C12-13-alkyl esters, potassium salts (CAS #91783-22-1)*: A pre-GLP ocular irritation test conducted according to OECD Guideline 405 was performed with New Zealand White rabbits (6 total) administered ocular instillations of 0.1 mL 50% w/w solutions of the test substance (44% active ingredient) in water. Half of the animals had their eyes rinsed 4 seconds after the instillation with 20 mL lukewarm water. The remaining

animals did not have their eyes rinsed. An observation period of 21 days followed the instillations. At 24, 48, and 72 hours, the mean corneal opacity score was 2/4, the mean iris score was 0.8/2, the mean conjunctival score was 2.1/3, and the mean chemosis score was 1.7/4 for the unrinsed eyes. Only the iris effects were fully reversible by the end of the observation period. At 21 days, the overall irritation scores were 0.66 and 0 for the unwashed and washed eyes, respectively. The authors concluded that the test substance was irritating to the eyes under the tested conditions (Klimisch Score 2, reliable with restrictions).

- *Surrogate: Sulfuric acid, mono-C10-16-alkyl esters, sodium salts (CAS #68585-47-7)*[9]*:* A non-GLP-compliant ocular irritation test conducted in a manner similar to OECD Guideline 405 was performed with New Zealand White rabbits (3 total) administered ocular instillations of 0.1 mL undiluted sulfuric acid, mono-C10-16-alkyl esters, sodium salts (10% active ingredient). An observation period of 7 days followed the instillations. At 24, 48, and 72 hours, the mean corneal opacity score was 1.4/4 (grade 1 in one animal), the mean iris score was 0.7/2, the mean conjunctival score was 2/3 (grade 1 in two animals), and the mean chemosis score was 1.6/4. The iris effects and chemosis were fully reversible while the corneal opacity and conjunctival redness were not fully reversible. The authors concluded that the test substance is irritating under CLP criteria (Klimisch Score 2, reliable with restrictions).
- *Surrogate: Sulfuric acid, mono-C10-16-alkyl esters, sodium salts (CAS #68585-47-7)*[10]*:* A non-GLP-compliant ocular irritation test conducted in a manner similar to OECD Guideline 405 was performed with New Zealand White rabbits (3 total) administered ocular instillations of 0.1 mL undiluted sulfuric acid, mono-C10-16-alkyl esters, sodium salts (10% active ingredient). A observation period of 14 days followed the instillations. At 24, 48, and 72 hours, the mean corneal opacity score was 0.9/4, the mean iris score was 0.7/2, the mean conjunctival score was 1.9/3, and the mean chemosis score was 1.6/4. All ocular irritation effects were fully reversible by the end of the observation period. The authors concluded that the test substance is not classified as irritating based on these results.
- Additionally studies presented in the REACH dossier were assigned Klimisch Scores of 3 (not reliable) or 4 (not assignable); therefore, ToxServices did not include the results of these studies in the present assessment.

- In summary, instillation of diluted solutions (5-6%) of sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate to the eyes of rabbits did not produce significant ocular irritation. In contrast, ocular instillation of more concentrated solutions of the surrogates sulfuric acid, mono-C12-16-alkyl esters, sodium salts; sulfuric acid, mono-C12-13-alkyl esters, potassium salts; and sulfuric acid, mono-C10-16-alkyl esters, sodium salts produced irritation effects that were not fully reversible by the end of the observation periods. Under GHS criteria (UN 2019), a chemical is classified as irritating to the eyes if it produces mean scores ≥ 1 for corneal opacity, ≥ 1 for iritis, ≥ 2 for conjunctival redness, and/or ≥ 2 for chemosis in at least 2 of 3 animals following readings at 24, 48, and 72 hours, with reversibility of the irritation effects occurring within 21 days (Category 2A) or 7 days (Category 2B). If the chemical produces irreversible effects to the cornea, iris, or conjunctiva within 21 days or produces corneal opacity scores ≥ 3 and/or iritis scores ≥ 1.5 in at least 2 of 3 testing animals following gradings at 24, 48, and 72 hours, the chemical is classified as a Category 1 eye irritant. As the surrogates sulfuric acid, mono-C12-16-alkyl esters, sodium salts and sulfuric acid, mono-C12-13-alkyl esters, potassium salts produced ocular irritation that was not fully reversible within 21 days, ToxServices classified sulfuric acid, mono-C12-18-

[9] The REACH dossier entry states that the test substance is SLS but the endpoint summary indicates CASRN 68585-47-7.
[10] The REACH dossier entry states that the test substance is SLS but the endpoint summary indicates CASRN 68585-47-7.

alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate as a GHS Category 1 eye irritant, in agreement with Australia's classification for this endpoint.

Ecotoxicity (Ecotox)

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of High for acute aquatic toxicity based on measured acute aquatic toxicity values as low as 1.3 mg/L for fish and 2.8 mg/L for aquatic invertebrates. GreenScreen® criteria classify chemicals as a High hazard for acute aquatic toxicity when acute aquatic toxicity values are > 1 to 10 mg/L (CPA 2018b). The confidence in the score is high as it is based on reliable measured data for all three trophic levels.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
  - 96-hour LC_{50} (*Danio rerio*, zebrafish) = 1.3 mg/L (nominal) (GLP-compliant, OECD Guideline 203) (Klimisch Score 1, reliable without restriction).
  - 96-hour LC_{50} (*Cyprinus carpio*, carp) = 17 mg/L (nominal) (GLP-compliant, EU Method C.1) (Klimisch Score 1, reliable without restriction).
  - 48-hour LC_{50} (*Leuciscus idus*, ide) = 9.3 mg/L (nominal) (non-GLP-compliant, DIN 38412/15) (Klimisch Score 2, reliable with restrictions).
  - 48-hour LC_{50} (*Leuciscus idus melanotus*, ide) = 16 mg/L (nominal) (non-GLP-compliant, DIN 38412, Teil 15) (Klimisch Score 2, reliable with restrictions).
  - 48-hour mobility EC_{50} (*Daphnia magna*) = 2.8 mg/L (nominal) (GLP-compliant, OECD Guideline 202) (Klimisch Score 1, reliable without restriction).
  - 48-hour mobility EC_{50} (*D. magna*) = 15 mg/L (nominal) (GLP-compliant, EU Method C.2) (Klimisch Score 1, reliable without restriction).
  - 48-hour mobility EC_{50} (*D. magna*) = 12 mg/L (nominal) (GLP-compliant, DIN 38412, Teil 11) (Klimisch Score 2, reliable with restrictions).
  - 72-hour EC_{50} (*Desmodesmus subspicatus*, algae) = 20 mg/L (growth rate), 14 mg/L (biomass) (both nominal) (GLP-compliant, EU Method C.3) (Klimisch Score 1, reliable without restriction).
  - 72-hour biomass and growth rate EC_{50} (*D. subspicatus*, algae) ≥ 3.09 mg/L (both measured) (GLP-compliant, OECD Guideline 201) (Klimisch Score 2, reliable with restrictions).
  - *Surrogate: Sodium lauryl sulfate (CAS #151-21-3):* 96-hour cell number EC_{50} (*D. subspicatus*, algae) = 38 mg/L (nominal) (GLP-compliant, DIN 38412, part 9) (Klimisch Score 2, reliable with restrictions).
  - Additionally studies presented in the REACH dossier were assigned Klimisch Scores of 4 (not assignable); therefore, ToxServices did not include the results of these studies in the present assessment.

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of High for chronic aquatic toxicity based on chronic aquatic toxicity values as low as 0.35 mg/L for fish, 0.14 mg/L for aquatic invertebrates, and 0.9 mg/L for algae. GreenScreen® criteria classify chemicals as a High hazard for chronic aquatic toxicity when chronic aquatic toxicity

values are > 0.1 to 1.0 mg/L (CPA 2018b). The confidence in the score is high as it is based on reliable measured data for all three trophic levels on strong surrogates.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
  - 21-day reproduction NOEC (*D. magna*) = < 1.3 mg/L (GLP-compliant, OECD Guideline 202) (Klimisch Score 2, reliable with restrictions).
  - 72-hour growth rate NOEC (*D. subspicatus*, algae) = 3 mg/L (nominal) (GLP-compliant, EU Method C.3) (Klimisch Score 1, reliable without restriction).
  - 72-hour biomass NOEC (*D. subspicatus*, algae) ≥ 3.09 mg/L (measured) (GLP-compliant, OECD Guideline 201) (Klimisch Score 2, reliable with restrictions).
  - *Surrogate: Sulfuric acid, mono-C14-18-alkyl esters, sodium salts (CAS #68081-98-1)*: 34-day larval weight/length/survival NOEC (*Pimephales promelas*, fathead minnow) = 0.35 mg/L (measured) (non-GLP-compliant, similar to OECD Guideline 210) (Klimisch Score 2, reliable with restrictions).
  - *Surrogate: Sulfuric acid, mono-C14-18-alkyl esters, sodium salts (CAS #68081-98-1)*: 35-day larval weight/length NOEC (*P. promelas*, fathead minnow) = 0.371 mg/L (measured) (GLP-compliant, OECD Series on Testing and Assessment, Number 53) (Klimisch Score 2, reliable with restrictions).
  - *Surrogate: Sodium lauryl sulfate (CAS #151-21-3):* 42-day weight/mortality NOEC (*P. promelas*, fathead minnow) > 1.357 mg/L (measured) (GLP status not specified) (Klimisch Score 2, reliable with restrictions).
  - *Surrogate: Sulfuric acid, mono-C12-15-alkyl esters, sodium salts (CAS #68890-70-0):* 21-day NOEC (*D. magna*) = 0.14 mg/L (mortality), 1.2 mg/L (reproduction) (both measured) (non-GLP-compliant OECD Guideline 202, part 2) (Klimisch Score 2, reliable with restrictions).
  - *Surrogate: Sodium lauryl sulfate (CAS #151-21-3):* 7-day NOEC (*Ceriodaphnia dubia*) = 0.88 mg/L (reproduction), 1.2 mg/L (mortality) (both measured) (non-GLP-compliant, similar to EPA-600/489/001) (Klimisch Score 2, reliable with restrictions).
  - *Surrogate: Sodium lauryl sulfate (CAS #151-21-3):* 96-hour cell number EC_0 (*D. subspicatus*, algae) = 0.9 mg/L (nominal) (GLP-compliant, DIN 38412, part 9) (Klimisch Score 2, reliable with restrictions).
  - Additionally studies presented in the REACH dossier were assigned Klimisch Scores of 4 (not assignable); therefore, ToxServices did not include the results of these studies in the present assessment.

Environmental Fate (Fate)

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Very Low for persistence based on it meeting the 10-day window in OECD Guideline 301 B and D ready biodegradation tests and water expected to be the dominant environmental compartment. GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when water is the dominant environmental compartment and the 10-day biodegradation window is met (CPA 2018b). The confidence in the score is high as it is based on reliable measured data.

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

  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
  - A GLP-compliant ready biodegradability test conducted according to EU Method C.4-C (CO_2 evolution) test was performed with non-adapted, activated domestic sludge exposed to sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (as C12-18-alkyl sulfate, sodium salt, 65.0% purity) at 44-45.3 mg/L (16.3-16.5 mg DOC/L) for 29 days. The 10-day window was achieved (no supporting data provided) and the test substance degraded 93% by the end of the exposure period. The positive control (sodium benzoate) achieved 86% degradation within 28 days. The authors concluded that the test substance was readily biodegradable under the tested conditions (Klimisch Score 1, reliable without restriction).
  - A non-GLP-compliant ready biodegradability test conducted in a manner similar to OECD Guideline 301 D (closed bottle test) was performed with non-adapted, activated domestic sludge exposed to sulfuric acid, mono-C12-18-alkyl esters, sodium salts (49.1% purity) at 1 or 2.5 mg/L for 30 days. At the end of the exposure period, the level of degradation was 74% and 111% for the 1 and 2.5 mg/L solutions, respectively. As the authors indicate that the 10-day window was met (no supporting data provided) and the reference substance (sulfuric acid, mono dodecyl ester sodium salt) achieved 93% degradation in 30 days, the authors concluded that the test substance was readily biodegradable under the tested conditions (Klimisch Score 2, reliable with restrictions).
  - A GLP-compliant ready biodegradability test conducted according to OECD Guideline 301 B (CO_2 evolution test) was performed with non-adapted, activated sludge (final effluent from a control, lab-scale sewage plant) exposed to sulfuric acid, mono-C12-18-alkyl esters, sodium salts (28.2% purity) at 10 or 20 mg/L for 28 days. The 10 and 20 mg/L test substance solutions degraded 79% and 84%, respectively, by the end of the exposure period. The 20 mg/L solution achieved 65% degradation by day 9, indicating that it met the 10-day window. The reference substance (sodium benzoate) achieved 100% degradation after 28 days. The authors concluded that the test substance was readily biodegradable under the tested conditions (Klimisch Score 1, reliable without restriction).
  - A non-GLP-compliant ready biodegradability test conducted according to OECD Guideline 301D (closed bottle test) was performed with non-adapted, activated sludge exposed to sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (36% purity) for 28 days. At the end of the exposure period, the test substance and reference substance (sodium benzoate) achieved 73% degradation. Additionally, the test substance achieved 70% degradation after 5 days, indicating that the 10-day window was met. The authors concluded that the test substance was readily biodegradable under the tested conditions (Klimisch Score 2, reliable with restrictions).
  - A GLP-compliant inherent biodegradability test conducted according to OECD Guideline 302 A (modified SCAS test) was performed with the mixed liquor and settled sewage effluent from municipal sweat treatment plants receiving mostly domestic sewage exposed to sulfuric acids, mono-C12-18-alkyl esters, sodium salts (33.7% aqueous paste) at 29 mg/L for 25 days. As the test substance achieved > 94% degradation by the end of the exposure period, the authors concluded that the test substance was inherently biodegradable under the tested conditions (Klimisch Score 2, reliable with restriction).
  - Additionally studies presented in the REACH dossier were assigned Klimisch Scores of 4 (not assignable); therefore, ToxServices did not include the results of these studies in the present assessment.

- OECD 2009
    - Based on their physicochemical properties, alkyl sulfates are expected to partition mostly in water (i.e., the hydrosphere). No partitioning to the atmosphere is expected due to their ionic structure. Alkyl sulfates are not expected to undergo hydrolysis in water due to the lack of hydrolysable functional groups.
    - Alkyl sulfates are readily biodegradable.

Bioaccumulation (B) Score (vH, H, M, L, or vL): vL
Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Very Low for bioaccumulation based on measured log K_{ow} values no greater than 1.41. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when log K_{ow}s are no greater than 4 (CPA 2018b). The confidence in the score is high as it is based on reliable measured data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate has a calculated log $K_{ow} \leq$ -2.1 at 20°C as identified using methods specified in OECD Guideline 107 (non-GLP-compliant).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate has a measured log K_{ow} of 1.41 at 24°C as identified in a non-GLP-compliant OECD Guideline 123 test
- ToxServices identified no bioaccumulation data for sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate. As modeling of environmental fate endpoints is not appropriate for chemicals with surfactant properties, ToxServices assigned the score for this endpoint based on the log K_{ow} values for this chemical.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *L*
Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Low for reactivity based on ToxServices not classifying them as reactive under GHS criteria. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when no GHS classifications are available (CPA 2018b). The confidence in the score is low as it is not based on measured data or authoritative listings.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (purity not specified) does not contain functional groups associated with explosive or oxidizing properties, and is not self-reactive.
- No measured data were identified. Therefore, screening procedures for explosivity were used here to estimate the reactivity property of sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate. These procedures are listed in the GHS (UN 2019).
    - Based on the structure of its components or moieties, sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is not considered

explosive or self-reactive due to lack of functional groups associated with explosive or self-reactive properties (See Appendix I).
    - Based on the structure of its components or moieties, sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is not considered to have oxidizing properties as it does not contain any structural groups known to be correlated with a tendency to react exothermally with combustible materials.
- Based on the above information, ToxServices did not classify Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate for reactivity under GHS criteria (UN 2019).

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

Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate was assigned a score of Moderate for flammability based on ToxServices classifying it as a Category 2 flammable solid under GHS criteria. GreenScreen® criteria classify chemicals as a Moderate hazard for flammability when they are classified as GHS Category 2 flammable solids (CPA 2018b). The confidence in the score was high as it is based on reliable measured data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (purity not specified) has a flash point of 160°C as identified in an EU Method A.9 test (GLP status not specified) (Klimisch Score 2, reliable with restrictions).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (purity not specified) has an auto-ignition temperature of 220°C as identified in a DIN 66165-2 test (GLP status not specified) (Klimisch Score 2, reliable with restrictions).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (as FAS C12-18, Na, purity not specified) took 24 seconds to burn as a 100 mm powder train (4.2 mm/s) in a non-GLP-compliant EU Method A.10 (flammability (solids)) test (Klimisch Score 1, reliable without restriction).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (light very fine powder, bulk density < 400 g/L, purity not specified) took 29 seconds to burn as a 100 mm powder train (3.4 mm/s) in a GLP-compliant UN Test N.1 study. The rate of burning over 200 mm was 58 seconds (Klimisch Score 1, reliable without restriction).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (solid material of bulk density < 400 g/L, purity not specified) took 43 seconds to burn as a 100 mm powder train (2.3 mm/s) in a GLP-compliant EU Method A.10 (flammability (solids)) test. The rate of burning over 200 mm was 84 seconds (Klimisch Score 1, reliable without restriction).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (solid material of bulk density > 400 g/L, purity not specified) took 83-96 seconds to burn as a 100 mm powder train (1.0-1.2 mm/s) in a GLP-compliant EU Method A.10 (flammability (solids)) test. The rate of burning over 200 mm was 135 seconds (Klimisch Score 1, reliable without restriction).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (solid material of bulk density > 400 g/L, purity not specified) took 55-84 seconds to burn as a 100 mm powder train (1.2-1.8 mm/s) in a GLP-compliant EU Method

A.10 (flammability (solids)) test. The rate of burning over 200 mm was 168 seconds (Klimisch Score 1, reliable without restriction).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate (as FAS C12-18, Na, purity not specified) took ~14.5 seconds to burn 100 mm (6.9 mm/s) in a non-GLP-compliant UN Method N.1 test. The wetted zone stopped the fire for slightly less than four minutes (Klimisch Score 2, reliable with restrictions).
    - Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is not pyrophoric, and does not liberate flammable gases in contact with water.
- As sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate is not flammable in contact with water and has burning times ≤ 43 seconds (equivalent to burning rates > 2.3 mm/s) in reliable flammability (solids) tests, ToxServices classified it as a Category 2 flammable solid under GHS criteria (UN 2019). GHS Category 2 flammable solids have burning times < 45 seconds or burning rates > 2.2 mm/second and are not flammable in contact with water.

Use of New Approach Methodologies (NAMs)[11] in the Assessment, Including Uncertainty Analyses of Input and Output

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

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

As shown in Table 5, Type I (input data) uncertainties in sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate's NAMs dataset include no *in vivo* and/or *in vitro* experimental data for endocrine activity and respiratory sensitization. Sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate's Type II (extrapolation output) uncertainties include limitations in the applicability domains of the (Quantitative) Structure Activity Relationship ((Q)SAR) models applied in this assessment and exogenous metabolic systems used in *in vitro* genotoxicity tests that do not entirely mirror *in vivo* metabolism. Some of sulfuric acid, mono-C12-18-alkyl esters, sodium salts / sodium pentadecyl sulfate / sodium coco sulfate's type II uncertainties were alleviated by the use of *in vitro* test batteries and/or in combination of *in vivo* data.

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

Uncertainty Analyses (OECD 2020b)	
Type I Uncertainty: Data/Model Input	**Endocrine activity**: No *in vivo* experimental data are available. **Respiratory sensitization**: No experimental data are available.
Type II Uncertainty: Extrapolation Output	**Genotoxicity:** The bacterial reverse mutation assay (as defined in OECD Guideline 471) only tests point-mutation inducing activity in non-mammalian cells, and the exogenous metabolic activation system does not entirely mimic *in vivo* conditions[12]. The mammalian cell gene mutation assay (as defined in OECD Guideline 476) only detects gene mutations, and the exogenous metabolic activation system does not entirely mirror *in vivo* metabolism (i.e. the liver S9 mix contains enzymes present in the endoplasmic reticulum but not the cytosol of liver cells).[13]

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

[12] https://www.oecd-ilibrary.org/docserver/9789264071247-en.pdf?expires=1614097593&id=id&accname=guest&checksum=89925F80B9F4BD2FFC6E90F94A0EE427

[13] https://www.oecd-ilibrary.org/docserver/9789264264809-en.pdf?expires=1614097800&id=id&accname=guest&checksum=C0DE371FB9C5A878E66C9AB7F84E6BBE

	Endocrine activity: ToxCast models don't define applicability domain; the *in vivo* relevance of EDSP Tox 21 screening assays and *in silico* models for receptor activities is unknown due to lack of consideration of metabolism and other toxicokinetic factors. **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* gene mutation assay
Reproductive toxicity	N	
Developmental toxicity	N	
Endocrine activity	Y	*In vitro* high throughput data: EDSP Tox 21 screening assays/ToxCast models/ Danish QSAR/VEGA
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	N	
Persistence	N	
Bioaccumulation	N	

References

Australian Industrial Chemicals Introduction Scheme (AICS). 2015. Selected anionic surfactants: Human health tier II assessment. Dated July 3, 2015. Department of Health, Australian Government. Available: https://www.industrialchemicals.gov.au/sites/default/files/Selected%20anionic%20surfactants_Human%20health%20tier%20II%20assessment.pdf

Chemical Classification and Information Database (CCID). 2021. Sodium mono-C12-18-alkyl sulphate (CAS #68955-19-1). Environmental Protection Authority, Government of New Zealand. Available: https://www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/6605

ChemIDplus. 2021. Sulfuric acid, mono-C12-18-alkyl esters, sodium salts (CAS #68955-19-1). United States National Library of Medicine. Available: https://chem.nlm.nih.gov/chemidplus/rn/68955-19-1

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

Danish Technical University (DTU). 2021. National Food Institute. Danish QSAR Database. Available: http://qsar.food.dtu.dk/.

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/10162/13632/information_requirements_r7a_en.pdf

European Chemicals Agency (ECHA). 2021a. REACH registration dossier for sulfuric acid, mono-C12-18-alkyl esters, sodium salts (CAS #68955-19-1). Available: https://echa.europa.eu/registration-dossier/-/registered-dossier/15009

European Chemicals Agency (ECHA). 2021b. REACH registration dossier for sodium dodecyl sulphate (CAS #151-21-3). Available: https://echa.europa.eu/registration-dossier/-/registered-dossier/2126

European Commission (EC). 2021. CosIng database entry for sodium C12-18 alkyl sulfate (CAS #68955-19-1). Available: https://ec.europa.eu/growth/tools-databases/cosing/index.cfm?fuseaction=search.details_v2&id=37765

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

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

Occupational Safety and Health Administration (OSHA). 2021. Permissible exposure limits – Annotated tables. Available: https://www.osha.gov/annotated-pels

Organisation for Economic Co-operation and Development (OECD). 2009. SIDS Initial Assessment Report for category of alkyl sulfates, alkane sulfonates and α-olefin sulfonates. Published December 2009. Available: https://hpvchemicals.oecd.org/ui/SIDS_Details.aspx?id=a6ffe5f3-0fc7-4394-8bfa-e5d50db648fd

Organisation for Economic Co-operation and Development (OECD). 2020a. OECD QSAR Toolbox for Grouping Chemicals into Categories Version 4.4.1. Available: http://toolbox.oasis-lmc.org/?section=download&version=latest.

Organization for Economic Co-operation and Development (OECD). 2020b. 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

Pharos. 2021. Pharos Chemical and Material Library entry for mono-C12-18-alkyl sulfate sodium salts (CAS #68955-19-1). Available: http://www.pharosproject.net/material/.

PubChem. 2021. Sulfuric acid, mono-C12-18-alkyl esters, sodium salts. United States National Library of Medicine. Available: https://pubchem.ncbi.nlm.nih.gov/compound/23700089

ToxServices. 2020. SOP 1.37: GreenScreen® Hazard Assessments. Dated: February 3, 2020.

United Nations (UN). 2019. Globally Harmonized System of Classification and Labelling of Chemicals (GHS). Eighth revised edition.

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

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

United States Environmental Protection Agency (U.S. EPA). 2015. Safer Choice Standard. Available: https://www.epa.gov/saferchoice/standard

United States Environmental Protection Agency (U.S. EPA). 2020a. Safer Chemical Ingredients List (SCIL). Available: https://www.epa.gov/saferchoice/safer-ingredients

United States Environmental Protection Agency (U.S. EPA). 2020b. 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/production/files/2020-06/documents/epa_nam_work_plan.pdf

United States Environmental Protection Agency (U.S. EPA). 2021. Endocrine Disruptor Screening Program (EDSP) Universe of Chemicals Dashboard. Available: https://comptox.epa.gov/dashboard/chemical_lists/EDSPUOC.

Virtual Models for Evaluating the Properties of Chemicals within a Global Architecture (VEGA). 2020. Predictive Model Platform version 1.1.5-b47. Available: http://www.vega-qsar.eu/index.php.

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 Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate (CAS #68955-19-1)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

GreenScreen® Score Inspector

Table 1: Hazard Table

			Group I Human					Group II and II* Human								Ecotox		Fate		Physical	
			Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
Table 2: Chemical Details									S	R *	S	R *	*	*								
Inorganic Chemical?	**Chemical Name**	**CAS#**	**C**	**M**	**R**	**D**	**E**	**AT**	**STs**	**STr**	**Ns**	**Nr**	**SNS***	**SNR***	**IrS**	**IrE**	**AA**	**CA**	**P**	**B**	**Rx**	**F**
No	**Sulfuric Acid, Mono-C12-18-Alkyl Esters,**	**68955-19-1**	**L**	**L**	*L*	**L**	DG	**L**	*M*	**L**	*M*	DG	**L**	*L*	**H**	**vH**	**H**	**H**	**vL**	**vL**	*L*	**M**

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	Yes	No
3	STOP						
4	STOP						

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Sulfuric Acid, Mono-C12-18-Alkyl Esters,	**2**

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

Table 6

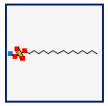
Chemical Name	Final GreenScreen® Benchmark Score
Sulfuric Acid, Mono-C12-18-Alkyl Esters,	**2**

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

Table 5: Data Gap Assessment Table

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

APPENDIX C: Pharos Output for Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate (CAS #68955-19-1)



68955-19-1

MONO-C12-18-ALKYL SULFATE SODIUM SALTS

ALSO CALLED Pentadecyl sodium sulfate, pentadecyl sodium sulfate, AldrichCPR, SODIUM C12-18 ALKYL SULFATE, SODIU...

View all synonyms (9)

Share Profile

Hazards | Properties | Functional Uses | Resources

All Hazards View

Show PubMed Results | Request Assessment | Add to Comparison

		Group I Human					Group II and II* Human									Ecotox			Fate		Physical		Mult	Non-GSLT			
	GS Score	C	M	R	D	E	AT	ST	ST	N	N	SnS	SnR	IrS	IrE	AA	CA	ATB	P	B	Rx	F	Mult	PBT	GW	O	Other
All Hazards	LT-P1	-	-	pC	-	-	M	pC	-	-	-	-	-	H	vH	pC	-	M	-	-	-	pC	pC	-	-	-	+

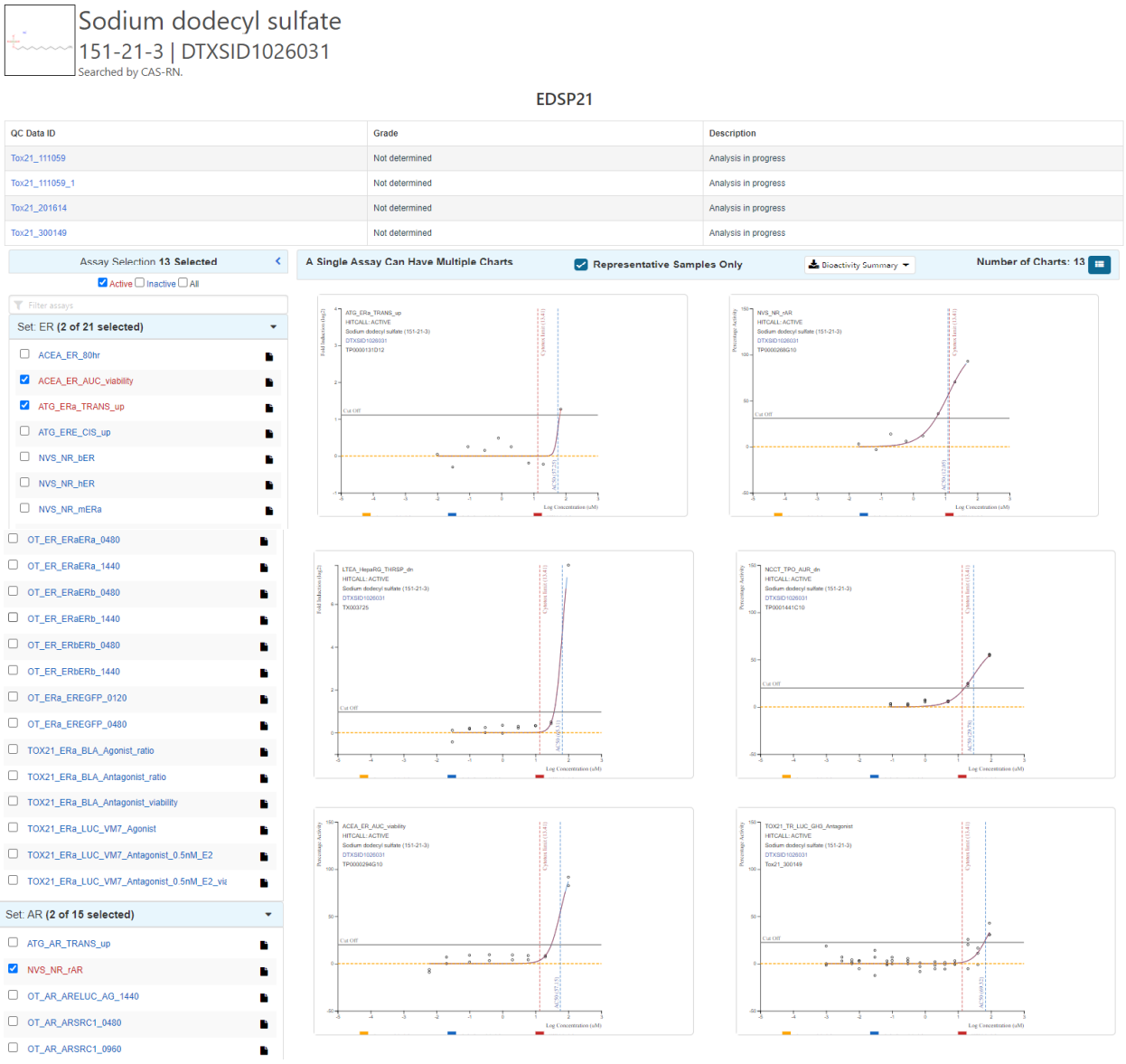
Hazard Lists

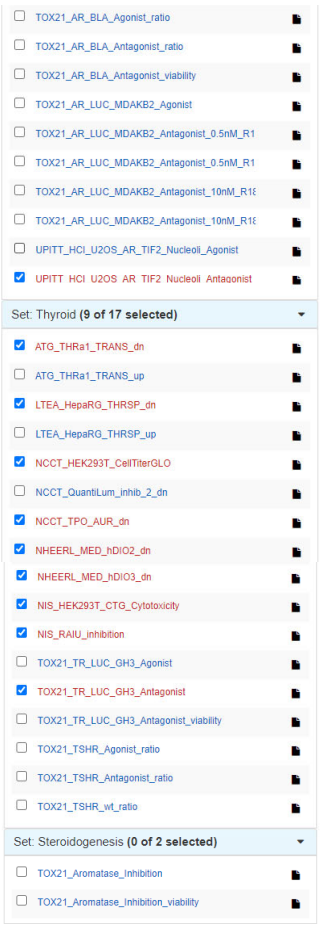
Download Lists

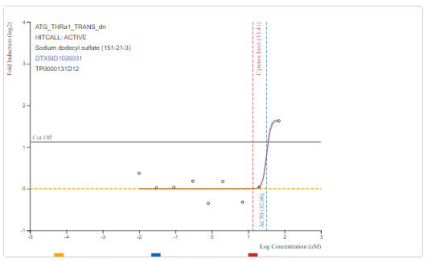
ENDPOINT	HAZARD LEVEL	GS SCORE	LIST NAME	HAZARD DESCRIPTION	OTHER LISTS
Reproductive Toxicity	pC	NoGS	DK-EPA - Danish Advisory List	Repr. 2; H361 - Suspected of damaging fertility or the unborn child (modeled)	
Acute Mammalian Toxicity	M	LT-UNK	GHS - New Zealand	6.1D (oral) - Acutely toxic	+1
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H302 - Harmful if swallowed (unverified)	
Systemic Toxicity/Organ Effects-Single Exposure	pC	NoGS	EU - Manufacturer REACH hazard submissions	H335 - May cause respiratory irritation (unverified)	
Skin Irritation/Corrosivity	H	LT-UNK	GHS - Australia	H315 - Causes skin irritation	+2
	H	LT-UNK	GHS - New Zealand	6.3A - Irritating to the skin (Cat. 2)	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H315 - Causes skin irritation (unverified)	

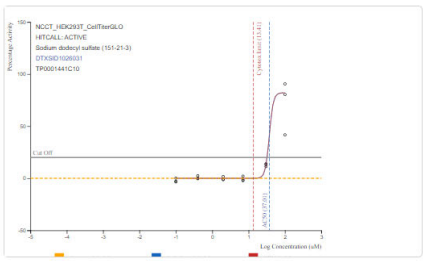
Eye Irritation/Corrosivity	vH	LT-UNK	GHS - Australia	H318 - Causes serious eye damage	+2
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H318 - Causes serious eye damage (unverified)	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H319 - Causes serious eye irritation (unverified)	
Acute Aquatic Toxicity	pC	NoGS	DK-EPA - Danish Advisory List	Aquatic Acute1 - Very toxic to aquatic life (modeled)	
Terrestrial Ecotoxicity	M	NoGS	GHS - New Zealand	9.3C - Harmful to terrestrial vertebrates	
Flammability	pC	NoGS	EU - Manufacturer REACH hazard submissions	H228 - Flammable solid (unverified)	
Human and/or Aquatic toxicity and/or Persistence and/or Bioaccumulation	U	LT-P1	German FEA - Substances Hazardous to Waters	Class 2 - Hazard to Waters	
T & P and/or B [(Chronic Aquatic Toxicity and Persistence) or (Acute Aquatic Toxicity and Persistence and/or Bioaccumulation)]	pC	NoGS	EU - Manufacturer REACH hazard submissions	H412 - Harmful to aquatic life with long lasting effects (unverified)	

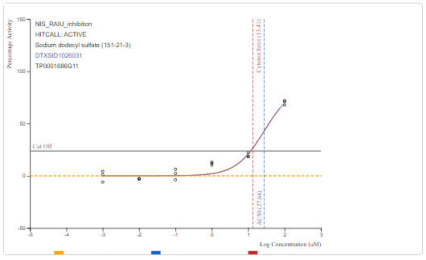
APPENDIX D: CompTox EDSP21 Results for the Surrogate Sodium Lauryl Sulfate (CAS #151-21-3)

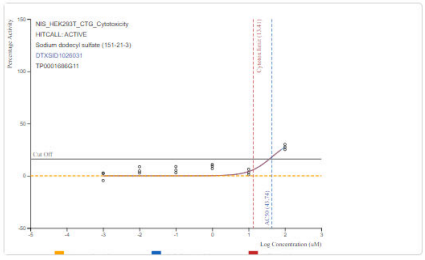


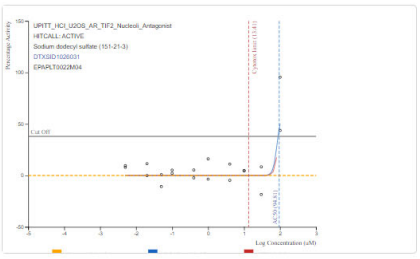


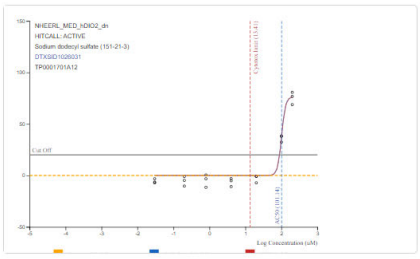


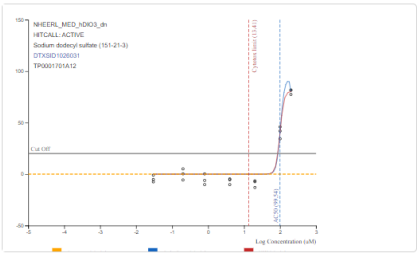




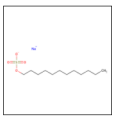








APPENDIX E: ToxCast Model Predictions for the Surrogate Sodium Lauryl Sulfate (CAS #151-21-3)



Sodium dodecyl sulfate
151-21-3 | DTXSID1026031
Searched by CAS-RN.

ToxCast: Models

ToxCast Model Predictions

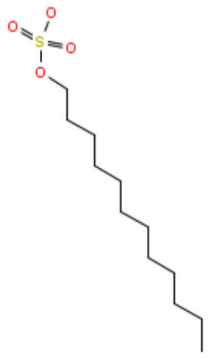
Download ToxCast Model Predictions

Model	Receptor	Agonist	Antagonist	Binding
ToxCast Pathway Model (AUC)	Androgen	0.00	5.49e-5	-
ToxCast Pathway Model (AUC)	Estrogen	0.00	0.00	-
COMPARA (Consensus)	Androgen	Inactive	Inactive	Inactive
CERAPP Potency Level (From Literature)	Estrogen	Inactive (Inactive)	-	Active (Very weak)
CERAPP Potency Level (Consensus)	Estrogen	Inactive (Inactive)	Active (VeryWeak)	Active (VeryWeak)

APPENDIX F: VEGA Endocrine Endpoint for the Surrogate Sodium Lauryl Sulfate (CAS #151-21-3)

1. Prediction Summary

Prediction for compound Molecule 0

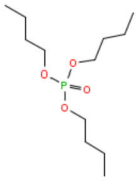


Prediction: Reliability:

Prediction is Active, but the result may be not reliable. A check of the information given in the following section should be done, paying particular attention to the following issues:
- only moderately similar compounds with known experimental value in the training set have been found
- similar molecules found in the training set have experimental values that disagree with the predicted value
- some atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments (2 infrequent fragments found)

Compound: Molecule 0
Compound SMILES: O=S(=O)([O-])OCCCCCCCCCCCC
Experimental value: -
Predicted activity: Active
Classification tree final node: 18
Reliability: the predicted compound is outside the Applicability Domain of the model
Remarks:
none

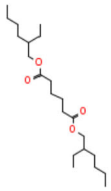
3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values



Compound #1

CAS: 126-73-8
Dataset id: 18 (Training set)
SMILES: O=P(OCCCC)(OCCCC)OCCCC
Similarity: 0.777

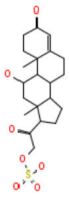
Experimental value: Inactive
Predicted value: Inactive



Compound #2

CAS: 103-23-1
Dataset id: 9 (Training set)
SMILES: O=C(OCC(CC)CCCC)CCCCC(=O)OCC(CC)CCCC
Similarity: 0.749

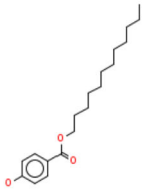
Experimental value: Inactive
Predicted value: Inactive



Compound #3

CAS: 100775-23-3
Dataset id: 139 (Training set)
SMILES: O=C3C=C2CCC1C4CCC(C(=O)COS(=O)(=O)O)C4(C)(CC(O)C1C2(C)CC3)
Similarity: 0.728

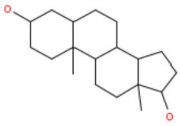
Experimental value: Inactive
Predicted value: Inactive



Compound #4

CAS: 2664-60-0
Dataset id: 220 (Training set)
SMILES: O=C(OCCCCCCCCCCCC)c1ccc(O)cc1
Similarity: 0.716

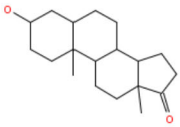
Experimental value: Active
Predicted value: Active



Compound #5

CAS: 571-20-0
Dataset id: 83 (Test set)
SMILES: OC4CCC2(C)(C(CCC1C3CCC(O)C3(C)(CCC12))C4)
Similarity: 0.714

Experimental value: Active
Predicted value: Active



Compound #6

CAS: 53-41-8
Dataset id: 78 (Training set)
SMILES: O=C2CCC3C4CCC1CC(O)CCC1(C)C4(CCC23(C))
Similarity: 0.711

Experimental value: Inactive
Predicted value: Active

3.2 Applicability Domain:
Measured Applicability Domain Scores

✖	**Global AD Index** AD index = 0 Explanation: the predicted compound is outside the Applicability Domain of the model.
⚠	**Similar molecules with known experimental value** Similarity index = 0.762 Explanation: only moderately similar compounds with known experimental value in the training set have been found.
✔	**Accuracy of prediction for similar molecules** Accuracy index = 1 Explanation: accuracy of prediction for similar molecules found in the training set is good.
✖	**Concordance for similar molecules** Concordance index = 0 Explanation: similar molecules found in the training set have experimental values that disagree with the predicted value.
✔	**Model's descriptors range check** Descriptors range check = True Explanation: descriptors for this compound have values inside the descriptor range of the compounds of the training set.
⚠	**Atom Centered Fragments similarity check** ACF index = 0.85 Explanation: some atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments (2 infrequent fragments found).

Symbols explanation:

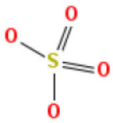
✔ The feature has a good assessment, model is reliable regarding this aspect.

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

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

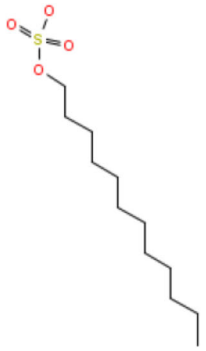
4.1 Reasoning:
Relevant Chemical Fragments and Moieties

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

	Fragment defined by the SMILES: O=S(=O)(O)O The fragment has less than 3 occurrences in the model's training set
	Fragment defined by the SMILES: OS The fragment has less than 3 occurrences in the model's training set

1. Prediction Summary

Prediction for compound Molecule 0

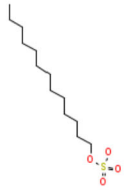


Prediction: Reliability:

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

Compound: Molecule 0
Compound SMILES: O=S(=O)([O-])OCCCCCCCCCCCC
Experimental value: -
Predicted ER-mediated effect: Not predicted
No. alerts for activity: 0
No. alerts for possible activity: 0
No. alerts for non-activity: 0
No. alerts for possible non-activity: 0
Structural alerts: -
Reliability: the predicted compound is outside the Applicability Domain of the model
Remarks:
none

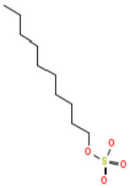
3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values



Compound #1

CAS: N.A.
Dataset id: 1014 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCCCCCC
Similarity: 0.976

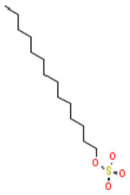
Experimental value: NON-active
Predicted value: Not predicted



Compound #2

CAS: N.A.
Dataset id: 682 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCCC
Similarity: 0.964

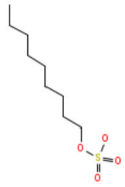
Experimental value: NON-active
Predicted value: Not predicted



Compound #3

CAS: N.A.
Dataset id: 889 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCCCCCCC
Similarity: 0.963

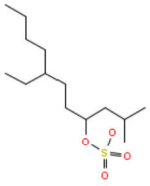
Experimental value: NON-active
Predicted value: Not predicted



Compound #4

CAS: N.A.
Dataset id: 874 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCC
Similarity: 0.947

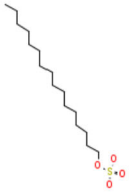
Experimental value: Active
Predicted value: Not predicted



Compound #5

CAS: N.A.
Dataset id: 661 (Training set)
SMILES: O=S(=O)(O)OC(CCC(CC)CCCC)CC(C)C
Similarity: 0.942

Experimental value: NON-active
Predicted value: Not predicted



Compound #6

CAS: N.A.
Dataset id: 683 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCCCCCCCC
Similarity: 0.94

Experimental value: NON-active
Predicted value: Not predicted

3.2 Applicability Domain:
Measured Applicability Domain Scores

✖	**Global AD Index** AD index = 0 Explanation: the predicted compound is outside the Applicability Domain of the model.
✔	**Similar molecules with known experimental value** Similarity index = 0.968 Explanation: strongly similar compounds with known experimental value in the training set have been found.
✖	**Accuracy of prediction for similar molecules** Accuracy index = 0 Explanation: accuracy of prediction for similar molecules found in the training set is not adequate.
✖	**Concordance for similar molecules** Concordance index = 0 Explanation: similar molecules found in the training set have experimental values that disagree with the predicted value.
✔	**Atom Centered Fragments similarity check** ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set.

Symbols explanation:

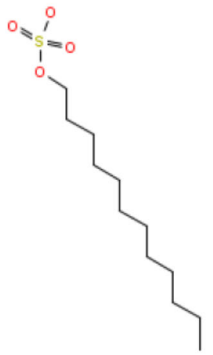
✔ The feature has a good assessment, model is reliable regarding this aspect.

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

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

1. Prediction Summary

Prediction for compound Molecule 0

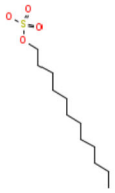


Prediction: Reliability:

Prediction is NON-active, the result appears reliable. Anyhow, you should check it through the evaluation of the information given in the following sections.
The following relevant fragments have been found: ER alert no. 27, inactive

Compound: Molecule 0
Compound SMILES: O=S(=O)([O-])OCCCCCCCCCCCC
Experimental value: -
Predicted AR binding activity: NON-active
No. alerts for binding activity: 0
No. alerts for non-binding activity: 1
Structural alerts: ER alert no. 27, inactive
Reliability: the predicted compound is into the Applicability Domain of the model
Remarks:
none

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

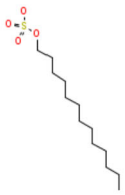


Compound #1

CAS: N.A.
Dataset id: 849 (Training set)
SMILES: CCCCCCCCCCCCOS(O)(=O)=O
Similarity: 0.988

Experimental value: NON-active
Predicted value: NON-active

Alerts (found also in the target): ER alert no. 27, inactive

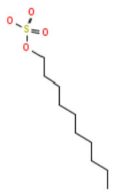


Compound #2

CAS: 3026-63-9
Dataset id: 1034 (Training set)
SMILES: CCCCCCCCCCCCCCOS(O)(=O)=O
Similarity: 0.976

Experimental value: NON-active
Predicted value: NON-active

Alerts (found also in the target): ER alert no. 27, inactive

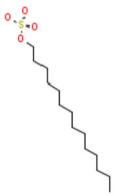


Compound #3

CAS: 142-87-0
Dataset id: 1179 (Training set)
SMILES: CCCCCCCCCCOS(O)(=O)=O
Similarity: 0.964

Experimental value: NON-active
Predicted value: NON-active

Alerts (found also in the target): ER alert no. 27, inactive

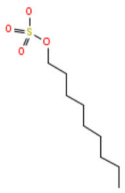


Compound #4

CAS: 1191-50-0
Dataset id: 999 (Training set)
SMILES: CCCCCCCCCCCCCCOS(O)(=O)=O
Similarity: 0.963

Experimental value: NON-active
Predicted value: NON-active

Alerts (found also in the target): ER alert no. 27, inactive



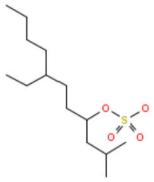
Compound #5

CAS: 1072-15-7
Dataset id: 1459 (Training set)
SMILES: CCCCCCCCCOS(O)(=O)=O
Similarity: 0.947

Experimental value: NON-active
Predicted value: NON-active

Alerts (found also in the target): ER alert no. 27, inactive

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



Compound #6

CAS: 139-88-8
Dataset id: 1268 (Training set)
SMILES: CC(C)CC(CCC(CCCC)CC)OS(O)(=O)=O
Similarity: 0.942

Experimental value: NON-active
Predicted value: NON-active

Alerts (found also in the target): ER alert no. 27, inactive

3.2 Applicability Domain:
Measured Applicability Domain Scores

Global AD Index
AD index = 0.991
Explanation: the predicted compound is into the Applicability Domain of the model.

Similar molecules with known experimental value
Similarity index = 0.982
Explanation: strongly similar compounds with known experimental value in the training set have been found.

Accuracy of prediction for similar molecules
Accuracy index = 1
Explanation: accuracy of prediction for similar molecules found in the training set is good.

Concordance for similar molecules
Concordance index = 1
Explanation: similar molecules found in the training set have experimental values that agree with the predicted value.

Atom Centered Fragments similarity check
ACF index = 1
Explanation: all atom centered fragment of the compound have been found in the compounds of the training set.

Symbols explanation:

The feature has a good assessment, model is reliable regarding this aspect.
The feature has a non optimal assessment, this aspect should be reviewed by an expert.
The feature has a bad assessment, model is not reliable regarding this aspect.

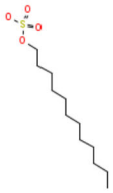
4.1 Reasoning:
Relevant Chemical Fragments and Moieties

(Molecule 0) Reasoning on fragments/structural alerts:

Fragment found: ER alert no. 27, inactive

Fragment related to ER inactivity (high reliability), defined by the SMARTS: CCOS(=O)

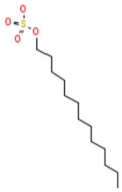
Following, the most similar compounds from the model's dataset having the same fragment.



CAS: N.A.
Dataset id: 849 (Training set)
SMILES: CCCCCCCCCCCCOS(O)(=O)=O
Similarity: 0.988

Experimental value: NON-active
Predicted value: NON-active

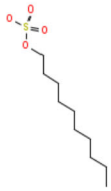
Alerts (found also in the target): ER alert no. 27, inactive



CAS: 3026-63-9
Dataset id: 1034 (Training set)
SMILES: CCCCCCCCCCCCCCOS(O)(=O)=O
Similarity: 0.976

Experimental value: NON-active
Predicted value: NON-active

Alerts (found also in the target): ER alert no. 27, inactive



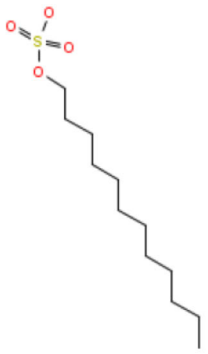
CAS: 142-87-0
Dataset id: 1179 (Training set)
SMILES: CCCCCCCCCCOS(O)(=O)=O
Similarity: 0.964

Experimental value: NON-active
Predicted value: NON-active

Alerts (found also in the target): ER alert no. 27, inactive

1. Prediction Summary

Prediction for compound Molecule 0

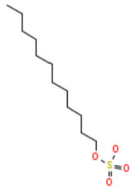


Prediction: Reliability:

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

Compound: Molecule 0
Compound SMILES: O=S(=O)([O-])OCCCCCCCCCCCC
Experimental value: -
Predicted TR alpha class: Inactive
Reliability: the predicted compound is into the Applicability Domain of the model
Remarks:
none

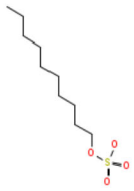
3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values



Compound #1

CAS: 151-21-3
Dataset id: 4205 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCCCCC
Similarity: 0.988

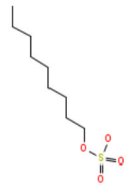
Experimental value: Inactive
Predicted value: Inactive



Compound #2

CAS: 142-87-0
Dataset id: 4204 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCCC
Similarity: 0.964

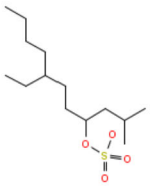
Experimental value: Inactive
Predicted value: Inactive



Compound #3

CAS: 1072-15-7
Dataset id: 4203 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCC
Similarity: 0.947

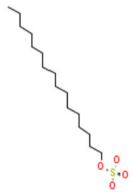
Experimental value: Inactive
Predicted value: Inactive



Compound #4

CAS: 139-88-8
Dataset id: 4200 (Training set)
SMILES: O=S(=O)(O)OC(CCC(CC)CCCC)CC(C)C
Similarity: 0.942

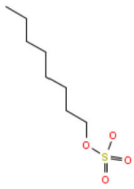
Experimental value: Inactive
Predicted value: Inactive



Compound #5

CAS: 1120-01-0
Dataset id: 4206 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCCCCCCCCC
Similarity: 0.94

Experimental value: Inactive
Predicted value: Inactive



Compound #6

CAS: 142-31-4
Dataset id: 4202 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCC
Similarity: 0.927

Experimental value: Inactive
Predicted value: Inactive

3.2 Applicability Domain:
Measured Applicability Domain Scores

Global AD Index
AD index = 0.982
Explanation: the predicted compound is into the Applicability Domain of the model.

Similar molecules with known experimental value
Similarity index = 0.965
Explanation: strongly similar compounds with known experimental value in the training set have been found.

Accuracy of prediction for similar molecules
Accuracy index = 1
Explanation: accuracy of prediction for similar molecules found in the training set is good.

Concordance for similar molecules
Concordance index = 1
Explanation: similar molecules found in the training set have experimental values that agree with the predicted value.

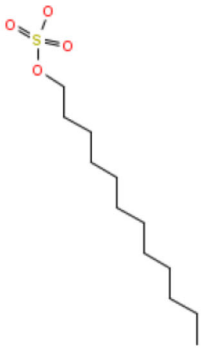
Atom Centered Fragments similarity check
ACF index = 1
Explanation: all atom centered fragment of the compound have been found in the compounds of the training set.

Symbols explanation:

The feature has a good assessment, model is reliable regarding this aspect.
The feature has a non optimal assessment, this aspect should be reviewed by an expert.
The feature has a bad assessment, model is not reliable regarding this aspect.

1. Prediction Summary

Prediction for compound Molecule 0

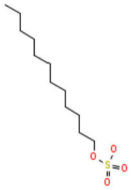


Prediction: Reliability:

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

Compound: Molecule 0
Compound SMILES: O=S(=O)([O-])OCCCCCCCCCCCC
Experimental value: -
Predicted TR beta class: Inactive
Reliability: the predicted compound is into the Applicability Domain of the model
Remarks:
none

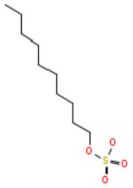
3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values



Compound #1

CAS: 151-21-3
Dataset id: 4223 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCCCCC
Similarity: 0.988

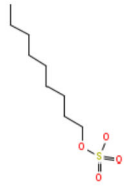
Experimental value: Inactive
Predicted value: Inactive



Compound #2

CAS: 142-87-0
Dataset id: 4222 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCCC
Similarity: 0.964

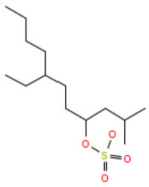
Experimental value: Inactive
Predicted value: Inactive



Compound #3

CAS: 1072-15-7
Dataset id: 4221 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCC
Similarity: 0.947

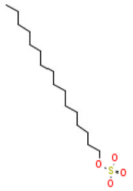
Experimental value: Inactive
Predicted value: Inactive



Compound #4

CAS: 139-88-8
Dataset id: 4218 (Training set)
SMILES: O=S(=O)(O)OC(CCC(CC)CCCC)CC(C)C
Similarity: 0.942

Experimental value: Inactive
Predicted value: Inactive



Compound #5

CAS: 1120-01-0
Dataset id: 4224 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCCCCCCCCCC
Similarity: 0.94

Experimental value: Inactive
Predicted value: Inactive

Compound #6

CAS: 142-31-4
Dataset id: 4220 (Training set)
SMILES: O=S(=O)(O)OCCCCCCCC
Similarity: 0.927

Experimental value: Inactive
Predicted value: Inactive

3.2 Applicability Domain:
Measured Applicability Domain Scores

Global AD Index
AD index = 0.982
Explanation: the predicted compound is into the Applicability Domain of the model.

Similar molecules with known experimental value
Similarity index = 0.965
Explanation: strongly similar compounds with known experimental value in the training set have been found.

Accuracy of prediction for similar molecules
Accuracy index = 1
Explanation: accuracy of prediction for similar molecules found in the training set is good.

Concordance for similar molecules
Concordance index = 1
Explanation: similar molecules found in the training set have experimental values that agree with the predicted value.

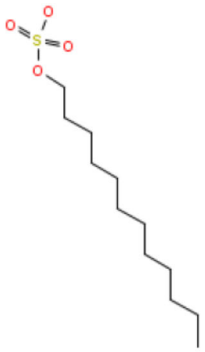
Atom Centered Fragments similarity check
ACF index = 1
Explanation: all atom centered fragment of the compound have been found in the compounds of the training set.

Symbols explanation:

The feature has a good assessment, model is reliable regarding this aspect.
The feature has a non optimal assessment, this aspect should be reviewed by an expert.
The feature has a bad assessment, model is not reliable regarding this aspect.

1. Prediction Summary

Prediction for compound Molecule 0

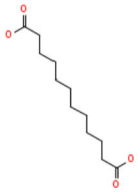


Prediction: Reliability:

Prediction is Inactive, but the result shows some critical aspects, which require to be checked:
- some atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments (1 infrequent fragments found)

Compound: Molecule 0
Compound SMILES: O=S(=O)([O-])OCCCCCCCCCCCC
Experimental value: -
Aromatase activity: Inactive
Probability(Active Agonist): 0.014
Probability(Active Antagonist): 0.038
Probability(Inactive): 0.948
Reliability: the predicted compound could be out of the Applicability Domain of the model
Remarks:
none

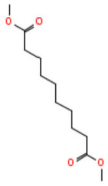
3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values



Compound #1

CAS: N.A.
Dataset id: 1553 (Test set)
SMILES: O=C(O)CCCCCCCCCC(=O)O
Similarity: 0.837

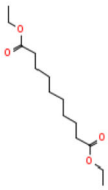
Experimental value: Inactive
Predicted value: Inactive



Compound #2

CAS: N.A.
Dataset id: 1510 (Training set)
SMILES: O=C(OC)CCCCCCCCC(=O)OC
Similarity: 0.825

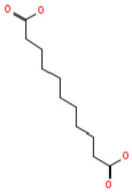
Experimental value: Inactive
Predicted value: Inactive



Compound #3

CAS: N.A.
Dataset id: 1461 (Test set)
SMILES: O=C(OCC)CCCCCCCCC(=O)OCC
Similarity: 0.824

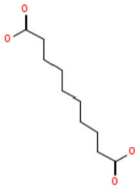
Experimental value: Inactive
Predicted value: Inactive



Compound #4

CAS: N.A.
Dataset id: 3102 (Test set)
SMILES: O=C(O)CCCCCCCCCC(=O)O
Similarity: 0.822

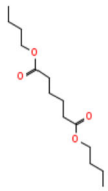
Experimental value: Inactive
Predicted value: Inactive



Compound #5

CAS: N.A.
Dataset id: 1372 (Test set)
SMILES: O=C(O)CCCCCCCCC(=O)O
Similarity: 0.806

Experimental value: Inactive
Predicted value: Inactive



Compound #6

CAS: N.A.
Dataset id: 1435 (Test set)
SMILES: O=C(OCCCC)CCCCC(=O)OCCCC
Similarity: 0.804

Experimental value: Inactive
Predicted value: Inactive

3.2 Applicability Domain:
Measured Applicability Domain Scores

Global AD Index
AD index = 0.775
Explanation: the predicted compound could be out of the Applicability Domain of the model.

Similar molecules with known experimental value
Similarity index = 0.831
Explanation: strongly similar compounds with known experimental value in the training set have been found.

Accuracy of prediction for similar molecules
Accuracy index = 1
Explanation: accuracy of prediction for similar molecules found in the training set is good.

Concordance for similar molecules
Concordance index = 1
Explanation: similar molecules found in the training set have experimental values that agree with the predicted value.

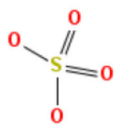
Atom Centered Fragments similarity check
ACF index = 0.85
Explanation: some atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments (1 infrequent fragments found).

Symbols explanation:

The feature has a good assessment, model is reliable regarding this aspect.
The feature has a non optimal assessment, this aspect should be reviewed by an expert.
The feature has a bad assessment, model is not reliable regarding this aspect.

4.1 Reasoning:
Relevant Chemical Fragments and Moieties

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



Fragment defined by the SMILES: O=S(=O)(O)O
The fragment has less than 3 occurrences in the model's training set

APPENDIX G: Danish (Q)SAR Endocrine and Molecular Endpoints for Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate (CAS #68955-19-1)

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Estrogen Receptor α Binding, Full training set (Human *in vitro*)		INC_OUT	NEG_OUT	NEG_OUT	NEG_OUT
Estrogen Receptor α Binding, Balanced Training Set (Human *in vitro*)		INC_OUT	INC_OUT	INC_OUT	NEG_OUT
Estrogen Receptor α Activation (Human *in vitro*)		INC_OUT	INC_OUT	NEG_OUT	POS_OUT
Estrogen Receptor Activation, CERAPP data (*in vitro*)		N/A	N/A	NEG_IN	N/A
Androgen Receptor Inhibition (Human *in vitro*)		INC_OUT	NEG_OUT	NEG_OUT	NEG_OUT
Androgen Receptor Binding, CoMPARA data (*in vitro*)		N/A	N/A	NEG_IN	N/A
Androgen Receptor Inhibition, CoMPARA data (*in vitro*)		N/A	N/A	NEG_IN	N/A
Androgen Receptor Activation, CoMPARA data (*in vitro*)		N/A	N/A	NEG_IN	N/A
Thyroperoxidase (TPO) inhibition QSAR1 (Rat *in vitro*)		N/A	N/A	NEG_IN	N/A
Thyroperoxidase (TPO) inhibition QSAR2 (Rat *in vitro*)		N/A	N/A	NEG_IN	N/A
Thyroid Receptor α Binding (Human *in vitro*)					
- mg/L				4067.683	
- µM				13186.21	
- Positive for IC_{50} ≤ 10 µM					
- Positive for IC_{50} ≤ 100 µM					
- Domain				OUT	OUT
Thyroid Receptor β Binding (Human *in vitro*)					
- mg/L				94.59911	
- µM				306.662	
- Positive for IC_{50} ≤ 10 µM					
- Positive for IC_{50} ≤ 100 µM					
- Domain				OUT	OUT
Arylhydrocarbon (AhR) Activation – Rational final model (Human *in vitro*)		N/A	N/A	INC_OUT	N/A
Arylhydrocarbon (AhR) Activation – Random final model (Human *in vitro*)		N/A	N/A	INC_OUT	N/A
Pregnane X Receptor (PXR) Binding (Human *in vitro*)	N/A	INC_OUT	INC_OUT	POS_OUT	NEG_OUT
Pregnane X Receptor (PXR) Binding (Human *in vitro*) NEW		N/A	N/A	INC_OUT	N/A
Pregnane X Receptor (PXR) Activation (Human *in vitro*)		N/A	N/A	NEG_IN	N/A

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Pregnane X Receptor (PXR) Activation (Rat *in vitro*)		N/A	N/A	NEG_IN	N/A
Constitutive Androstane Receptor (CAR) Activation at max. 20 µM (*in vitro*)		N/A	N/A	NEG_IN	N/A
Constitutive Androstane Receptor (CAR) Activation at max. 50 µM (*in vitro*)		N/A	N/A	NEG_IN	N/A
Constitutive Androstane Receptor (CAR) Inhibition at max. 20 µM (*in vitro*)		N/A	N/A	NEG_IN	N/A
Constitutive Androstane Receptor (CAR) Inhibition at max. 50 µM (*in vitro*)		N/A	N/A	NEG_IN	N/A
	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
CYP3A4 Induction (Human *in vitro*)		N/A	N/A	NEG_IN	N/A

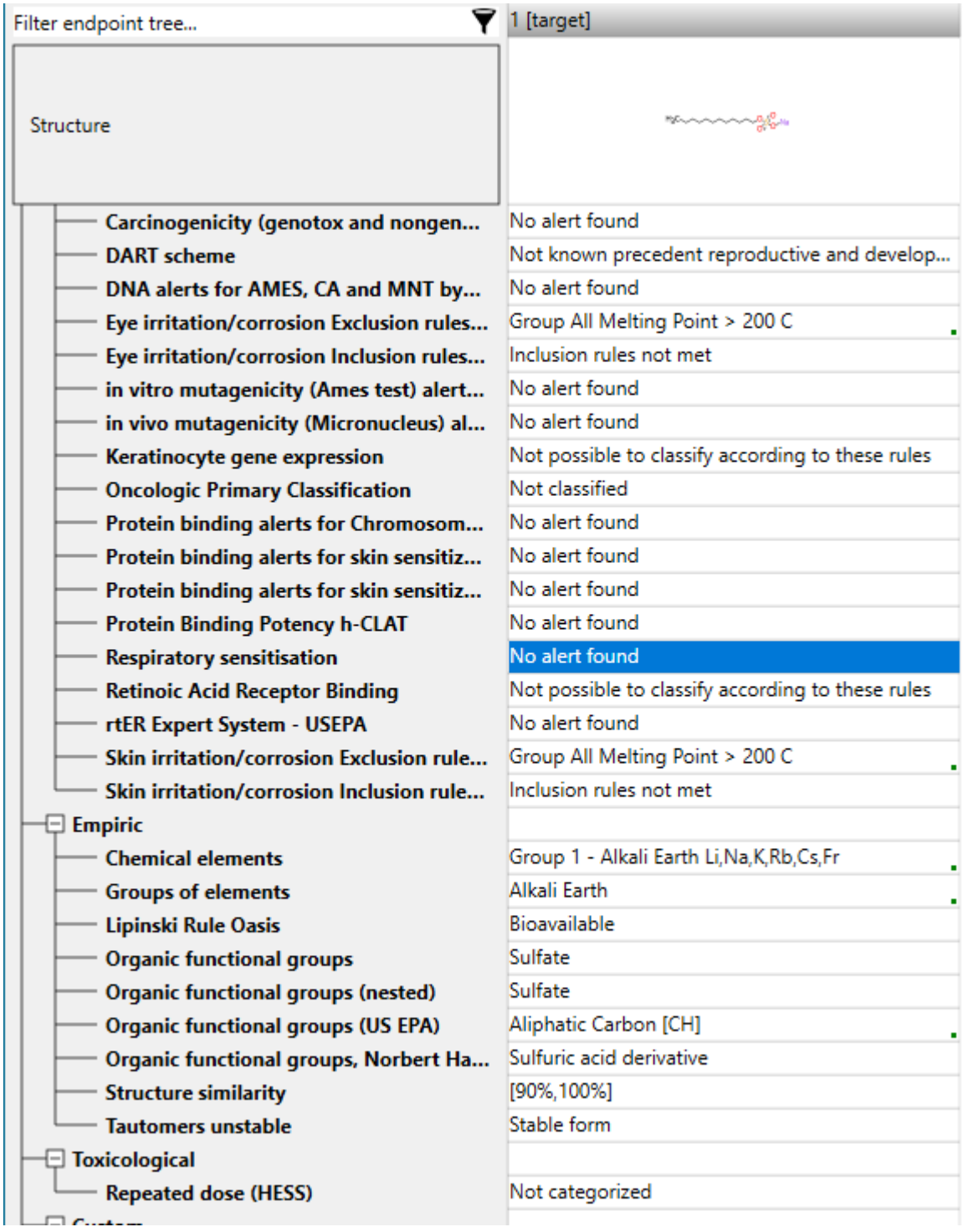
DTU-developed models

Estrogen Receptor Binding, alerts in:	
- parent only	Non binder, non cyclic structure
- metabolites from *in vivo* Rat metabolism simulator only	
- metabolites from Rat liver S9 metabolism simulator only	Non binder, non cyclic structure
rtER Expert System - USEPA, alerts in:	
- parent only	No alert found
- metabolites from *in vivo* Rat metabolism simulator only	
- metabolites from Rat liver S9 metabolism simulator only	No alert found

OECD QSAR Toolbox v.4.2 profilers

Profiler predictions are supporting information to be used together with the relevant QSAR predictions

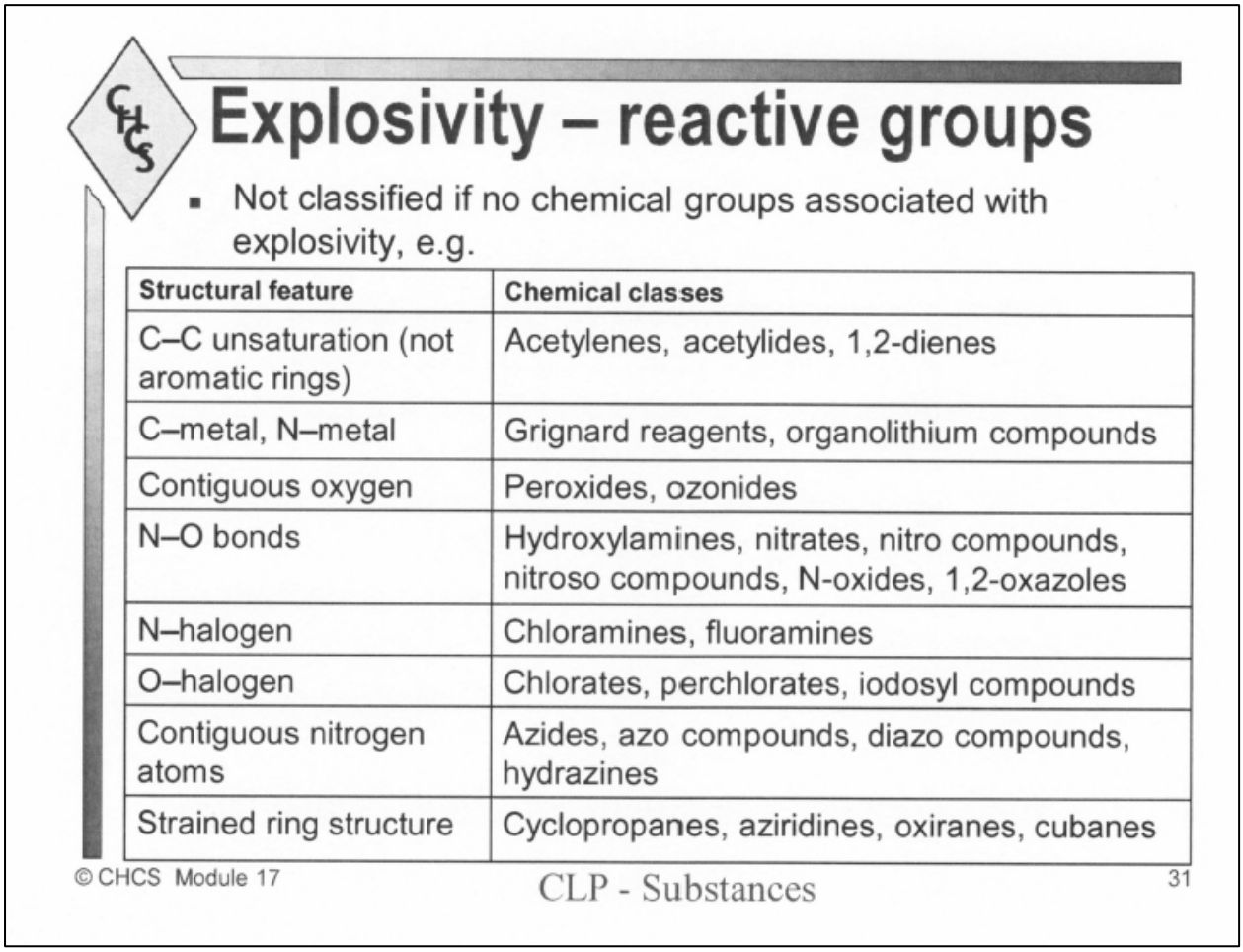
APPENDIX H: OECD Toolbox Respiratory Sensitization Results for Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate (CAS #68955-19-1)



Filter endpoint tree...	1 [target]
Structure	
Carcinogenicity (genotox and nongen...	No alert found
DART scheme	Not known precedent reproductive and develop...
DNA alerts for AMES, CA and MNT by...	No alert found
Eye irritation/corrosion Exclusion rules...	Group All Melting Point > 200 C
Eye irritation/corrosion Inclusion rules...	Inclusion rules not met
in vitro mutagenicity (Ames test) alert...	No alert found
in vivo mutagenicity (Micronucleus) al...	No alert found
Keratinocyte gene expression	Not possible to classify according to these rules
Oncologic Primary Classification	Not classified
Protein binding alerts for Chromosom...	No alert found
Protein binding alerts for skin sensitiz...	No alert found
Protein binding alerts for skin sensitiz...	No alert found
Protein Binding Potency h-CLAT	No alert found
Respiratory sensitisation	No alert found
Retinoic Acid Receptor Binding	Not possible to classify according to these rules
rtER Expert System - USEPA	No alert found
Skin irritation/corrosion Exclusion rule...	Group All Melting Point > 200 C
Skin irritation/corrosion Inclusion rule...	Inclusion rules not met
Empiric	
Chemical elements	Group 1 - Alkali Earth Li,Na,K,Rb,Cs,Fr
Groups of elements	Alkali Earth
Lipinski Rule Oasis	Bioavailable
Organic functional groups	Sulfate
Organic functional groups (nested)	Sulfate
Organic functional groups (US EPA)	Aliphatic Carbon [CH]
Organic functional groups, Norbert Ha...	Sulfuric acid derivative
Structure similarity	[90%,100%]
Tautomers unstable	Stable form
Toxicological	
Repeated dose (HESS)	Not categorized

APPENDIX I: Known Structural Alerts for Reactivity

Explosivity – Abbreviated List



Explosivity – reactive groups

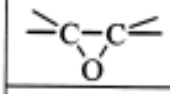
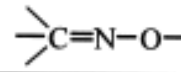
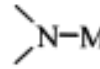
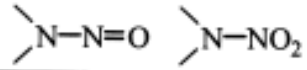
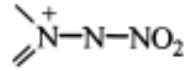
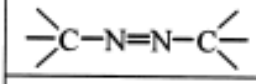
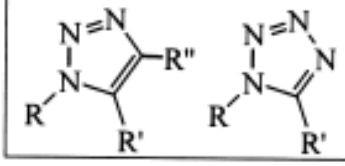
- Not classified if no chemical groups associated with explosivity, e.g.

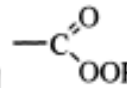
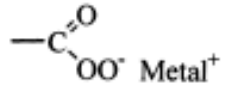
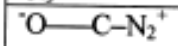
Structural feature	Chemical classes
C–C unsaturation (not aromatic rings)	Acetylenes, acetylides, 1,2-dienes
C–metal, N–metal	Grignard reagents, organolithium compounds
Contiguous oxygen	Peroxides, ozonides
N–O bonds	Hydroxylamines, nitrates, nitro compounds, nitroso compounds, N-oxides, 1,2-oxazoles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

© CHCS Module 17 CLP - Substances 31

Explosivity – Full List

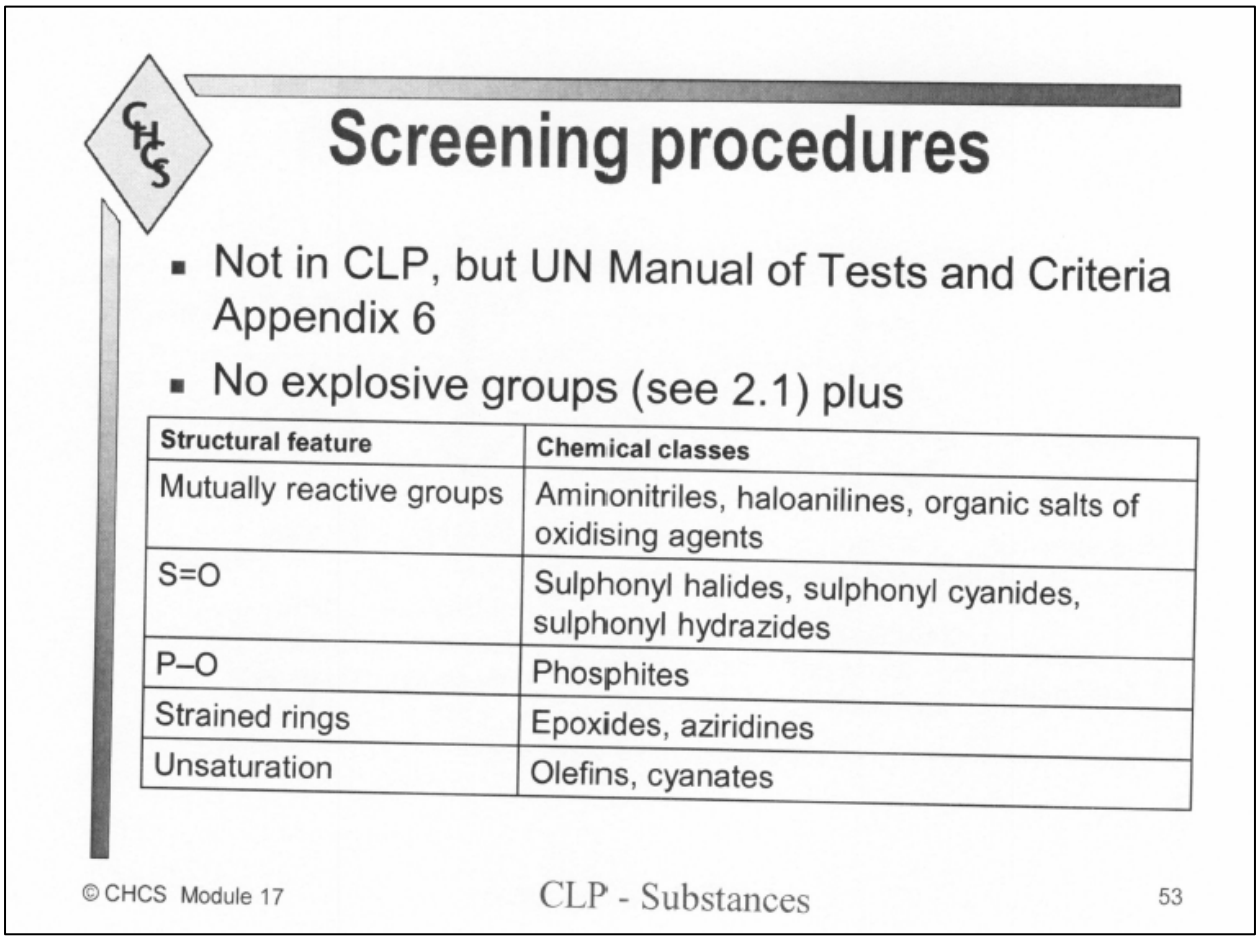
Table R.7.1-28 Chemical groups associated with explosive properties

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

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

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

Self-Reactive Substances



Screening procedures

- Not in CLP, but UN Manual of Tests and Criteria Appendix 6
- No explosive groups (see 2.1) plus

Structural feature	Chemical classes
Mutually reactive groups	Aminonitriles, haloanilines, organic salts of oxidising agents
S=O	Sulphonyl halides, sulphonyl cyanides, sulphonyl hydrazides
P–O	Phosphites
Strained rings	Epoxides, aziridines
Unsaturation	Olefins, cyanates

Licensed GreenScreen® Profilers

Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate GreenScreen® Evaluation Prepared by:

SIGNATURE BLOCK

Zach Guerrette, Ph.D., D.A.B.T.
Senior Toxicologist
ToxServices LLC

Sulfuric Acid, Mono-C12-18-Alkyl Esters, Sodium Salts / Sodium Pentadecyl Sulfate / Sodium Coco Sulfate GreenScreen® Evaluation QC'd by:

SIGNATURE BLOCK

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