# DODECYL ALCOHOL, ETHOXYLATED (EO < 10)

## (CAS #9002-92-0)

## GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

**Prepared by:**

**ToxServices LLC**

**Assessment Date: August 28, 2023**

**Expiration Date: August 28, 2028**

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

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## GreenScreen® Executive Summary for Dodecyl Alcohol, Ethoxylated (EO < 10) (CAS #9002-92-0)

Dodecyl alcohol, ethoxylated (EO < 10) is a group of C12 linear alcohol ethoxylates (AEs) with an average of 1 to 9 ethylene oxide (EO) units. Dodecyl alcohol, ethoxylated (EO < 10) belongs to the chemical category of polyethylene glycol (PEG) ethers, which function as surfactants across numerous industries. Additionally, dodecyl alcohol, ethoxylated (EO < 10) (CAS #9002-92-0) is approved by the United States Food and Drug Administration (U.S. FDA) for indirect food additive uses as an adjuvant and production aid under 21 CFR §178.3760. The CAS number 9002-92-0 refers to AEs with one 12-carbon chain and any number of EO units. The scope of this GreenScreen® is limited to C12 AEs with < 10 EO units.

Dodecyl alcohol, ethoxylated (EO < 10) is liquid at standard temperature and pressure. Based on its boiling point of 242°C, it is a volatile organic compound (VOC). It has moderate solubility in water (281.1 mg/L). Dodecyl alcohol, ethoxylated (EO < 10) is not flammable, explosive, or oxidizing.

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes"). This score is based on the following hazard score:

- Benchmark 2e
    - Moderate Group I Human Toxicity (developmental toxicity-D)

A data gap (DG) exists for endocrine activity-E. As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), dodecyl alcohol, ethoxylated (EO < 10) meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gap. In a worst-case scenario, if dodecyl alcohol, ethoxylated (EO < 10) were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

New Approach Methodologies (NAMs) used in this GreenScreen® include *in silico* modeling for carcinogenicity, endocrine activity, and respiratory sensitization, and a variety of *in vitro* studies for genotoxicity, skin irritation, and eye irritation. 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 dodecyl alcohol, ethoxylated (EO < 10)'s NAMs dataset include limited experimental data for carcinogenicity, endocrine activity, and respiratory sensitization, and lack of established test methods for respiratory sensitization. Dodecyl alcohol, ethoxylated (EO < 10)'s Type II (extrapolation output) uncertainties include lack of defined applicability domains of OECD QSAR Toolbox and ToxCast models in examination of structural alerts, limitation of in vitro genotoxicity assays in mimicking *in vivo* metabolism and their focusing on one or only a few types of genotoxicity events, uncertain *in vivo* relevance of *in silico* receptor binding activity predictions, the limitations in the examination of structural alerts for respiratory sensitization evaluation that does not account for non-immunologic mechanisms of respiratory sensitization, and inability of individual in vitro skin irritation and eye irritation tests to completely differentiate certain GHS categories. Some of dodecyl alcohol, ethoxylated (EO < 10)'s type II uncertainties were alleviated by the use of *in vitro* test batteries and/or in combination of *in vivo* data.

**GreenScreen® Hazard Summary Table for Dodecyl Alcohol, Ethoxylated (EO < 10)**

| 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** | *M* | DG | **M** | *M* | **L** | *L* | *M* | **L** | *L* | **L** | *H* | **H** | *H* | *vL* | *vL* | *L* | **L** |

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

# GreenScreen® Chemical Assessment for Dodecyl Alcohol, Ethoxylated (EO < 10) (CAS #9002-92-0)

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

**GreenScreen® Assessment (v.1.4) Prepared By:**
Name: Deb Remeikas, M.A.
Title: Toxicologist
Organization: ToxServices LLC
Date: July 25, 2023

**Quality Control Performed By:**
Name: Bingxuan Wang, Ph.D., D.A.B.T.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: August 28, 2023

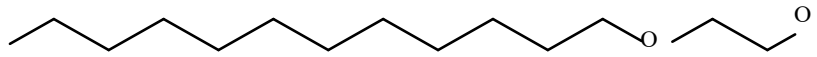
Expiration Date: August 28, 2023[2]

**Chemical Name:** Dodecyl alcohol, ethoxylated (EO < 10)

**CAS Number:** 9002-92-0 (generic)

**Chemical Structure(s):**

The CAS number 9002-92-0 refers to alcohol ethoxylates (AEs) with one 12-carbon chain and any number of EO units. The scope of this GreenScreen® is limited to C12 AEs with < 10 EO units. A representative structure for the target chemical with 1 EO is presented below (DTU 2023).



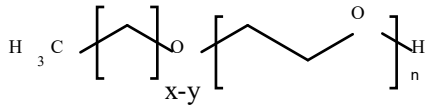

*SMILES: C(CCCCCCCCCCC)OCCO* (DTU 2023)

**Also called:** PEG lauryl ether, Alpha-dodecyl-omega-hydroxypoly(oxyethylene); Polyethylene glycol monododecyl ether; PEG dodecyl ether; Dodecyl poly(oxyethylene) ether; Laureth; PEG monolauryl ether; Dodecyl alcohol ethylene oxide; Poly(oxy-1,2-ethanediyl), alpha-dodecyl-omega-hydroxy-; Alpha-dodecyl-omega-hydroxypoly(oxy-1,2-ethanediyl); Dodecyl alcohol, monoether with polyethylene glycol; Lauryl alcohol, ethoxylated; Ethylene oxide-lauryl alcohol polycondensate; Alpha-dodecanol-omega-hydroxypoly(oxyethylene) (U.S. FDA 2023). Tradename: NOIGEN ET-83 (ECHA 2023a).

**Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):**
Limited data were available regarding the toxicity of dodecyl alcohol, ethoxylated (EO < 10). Therefore, linear alcohol ethoxylates (AEs) with a similar number of carbons (C12) and ethoxylate units < 10 were used as surrogates. For aquatic toxicity and bioaccumulation, compounds with carbon lengths ranging from 9 to 16 and EO < 10 were considered the most similar and best surrogates, but the ranges were extended as needed due to data availability and to depict trends. For environmental persistence, surrogates with longer carbon chain lengths and EO units were also included as they are

[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).

expected to biodegrade more slowly and are therefore conservative surrogates. AEs can be represented by the generic structure below.




x-y : Range of carbon units

n : Avergae number of ethylene oxide units

**Identify Applications/Functional Uses** (HERA 2009, CIR 2012, EC 2023)**:**
1. Surfactant – emulsifying and cleaning, across multiple industries,
2. Fragrances in cosmetic formulations,
3. Cleansing agents in cosmetic formulations,
4. Antistatic agents in cosmetic formulations.

**Known Impurities:**
Common impurities of dodecyl alcohol, ethoxylated (EO < 10), particularly laureths, include trace amounts of unreacted ethylene oxide (CAS #75-21-8) and 1,4-dioxane (CAS #123-91-1), a reaction product of ethoxylation (CIR 2012). According to the GreenScreen® Guidance, impurities present at < 100 ppm require a List Translator screening, while those present at > 100 ppm require separate full GreenScreen® evaluations. Ethylene oxide and 1,4-dioxane are LT-1 chemicals. Impurities are not evaluated in this assessment. Instead, they are evaluated at the product level, should they be present at > 100 ppm.

**GreenScreen® Summary Rating for Dodecyl Alcohol, Ethoxylated (EO < 10)**[3,4 5,6]**:** Dodecyl alcohol, ethoxylated (EO < 10) 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:
- Benchmark 2e
    - Moderate Group I Human Toxicity (developmental toxicity-D)

A data gap (DG) exists for endocrine activity-E. As outlined in GreenScreen® Guidance (CPA 2018b) Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), dodecyl alcohol, ethoxylated (EO < 10) meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gap. In a worst-case scenario, if dodecyl alcohol, ethoxylated (EO < 10) were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

[3] 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.
[4] See Appendix A for a glossary of hazard endpoint acronyms.
[5] For inorganic chemicals only, see GreenScreen® Guidance v1.4 Section 12 (Inorganic Chemical Assessment Procedure).
[6] For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen® Guidance v1.4 Annex 2.

**Figure 1: GreenScreen® Hazard Summary Table for Dodecyl Alcohol, Ethoxylated (EO < 10)**

| 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 | *M* | DG | **M** | *M* | L | *L* | *M* | L | *L* | L | *H* | **H** | *H* | *vL* | *vL* | *L* | L |

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

## Environmental Transformation Products

Per GreenScreen® guidance (CPA 2018b), chemicals that degrade rapidly and completely (i.e., meet criteria for a Very Low for persistence) are not likely to form persistent biodegradation intermediates because the degradation intermediates will not persist long enough to be encountered after use or release of the parent chemical (i.e., relevant). As dodecyl alcohol, ethoxylated (EO < 10) is readily biodegradable, it is not expected to have relevant transformation products.

## Introduction

Dodecyl alcohol, ethoxylated (EO < 10) represents a group of 12-carbon chain alcohol ethoxylates (AEs) that have less than 10 ethoxylation units. They are used primarily as surfactants and are produced via ethoxylation of primary alcohols with EO using base catalyzed reactions with potassium or sodium hydroxide followed by neutralization with an acid (HERA 2009).

ToxServices assessed dodecyl alcohol, ethoxylated (EO < 10) against GreenScreen® Version 1.4 (CPA 2018b) following procedures outlined in ToxServices' SOPs (GreenScreen® Hazard Assessment) (ToxServices 2021).

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

The SCIL is a list of chemicals that meet the Safer Choice standard (U.S. EPA 2023a). 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).

Dodecyl alcohol, ethoxylates (CAS #9002-92-0) are listed on the U.S. EPA SCIL as acceptable surfactants as a full green circle; however, no information was provided on specific number of EO units.

## 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 2023) 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),[7] 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

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

scores for each human health and environmental endpoint. The output for dodecyl alcohol, ethoxylated (EO < 10) can be found in Appendix C.

- Dodecyl alcohol, ethoxylated (EO < 10) is an LT-P1 chemical when screened using Pharos, and therefore a full GreenScreen® is required.
- Dodecyl alcohol, ethoxylated (EO < 10) [is not listed on the U.S. DOT list.
- Dodecyl alcohol, ethoxylated (EO < 10) is on the following lists for multiple endpoints. Specified lists for single endpoints are reported in individual hazard endpoints in the hazard assessment section below.
    - EC - CEPA DSL - Inherently Toxic in the Environment (iTE)
    - EC - CEPA DSL - Inherently Toxic to Humans (iTH)
    - German FEA - Substances Hazardous to Waters - Class 2 - Hazard to Waters

**Hazard Statement and Occupational Control**

No Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statements were identified for dodecyl alcohol, ethoxylated (EO < 10); self-classifications by authors of the REACH dossier for EO 1-2.5 and by the majority of notifiers (EO number unspecified) are indicated in Table 1. General personal protective equipment (PPE) recommendations are presented in Table 2, below. No occupational exposure limits (OELs) were identified.

**Table 1: GHS H Statements for Dodecyl Alcohol, Ethoxylated (EO < 10) (CAS #9002-92-0) (ECHA 2023a,b)**

| H Statement | H Statement Details |
|---|---|
| H302 | Harmful if swallowed. |
| H319 | Causes serious eye irritation. |
| H412 | Harmful to aquatic life with long lasting effects. |

**Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for Dodecyl Alcohol, Ethoxylated (EO < 10) (CAS #9002-92-0)**

| Personal Protective Equipment (PPE) | Reference | Occupational Exposure Limits (OEL) | Reference |
|---|---|---|---|
| Appropriate eye protection, protective clothing. No respiratory protection is required, except when aerosols/vapors are generated. | Sigma-Aldrich 2022 | None identified | Sigma-Aldrich 2022 |

**Physicochemical Properties of Dodecyl Alcohol, Ethoxylated (EO < 10)**

Dodecyl alcohol, ethoxylated (1-2.5 EO) is a colorless liquid at standard temperature and pressure. Its vapor pressure ($1.77 \times 10^{-5}$ mmHg) indicates that it will exist in the liquid and vapor phases. The water solubility and partition coefficient of linear AEs vary by the number of EO units, with longer EO chains increasing the water solubility (HERA 2009). A boiling point in the range of 111 to 121°C was reported for dodecyl alcohol, ethoxylated (1-2.5 EO), indicating it is volatile. Dodecyl alcohol, ethoxylated (1-2.5 EO) is moderately soluble in water (281.1 mg/L). It is more soluble in octanol than water (log $K_{ow}$ of 2.26).

| Table 3: Physical and Chemical Properties of Dodecyl Alcohol, Ethoxylated* (EO < 10) (CAS #9002-92-0) | | |
|---|---|---|
| **Property** | **Value** | **Reference** |
| Molecular formula | Multiple; $(C_2H_4O)_xC_{12}H_{26}O$ | HSDB 2018 |
| SMILES Notation | Multiple | ECHA 2023a |
| Molecular weight | Varies | ECHA 2023a |
| Physical state | Liquid | ECHA 2023a |
| Appearance | Colorless to yellow | HSDB 2018 |
| Melting point | -5.37°C at 97.8 kPa (equiv. to 733.8 mmHg) (exp) | ECHA 2023a |
| Boiling point | 242°C at 96.9 kPa (equiv. to 727.1 mmHg) (exp, OECD Guideline 103) | ECHA 2023a |
| Vapor pressure | 1.77 x $10^{-5}$ mmHg at 25°C (est) | ECHA 2023a |
| Water solubility | 281.1 mg/L at 25°C (exp., OECD Guideline 105) | ECHA 2023a |
| Dissociation constant | pKa at 20°C = 0 (exp., ISO/IEC 17025) | ECHA 2023a |
| Density/specific gravity | 0.906 at 20°C (exp., OECD Guideline 109) | ECHA 2023a |
| Partition coefficient | 2.26 at 25°C (exp., OECD Guideline 117) | ECHA 2023a |
| Supplier, Tradename(s) | None identified | |
| Ethoxylated or propoxylated? | Ethoxylated | |
| # EO Units | < 10 | |
| # PO Units | None | |
| EO/PO Ratio | None | |

*Chemical properties are based on dodecyl alcohol, ethoxylated (1-2.5 EO) (ECHA 2023a).

**Toxicokinetics**

Absorption, distribution, metabolism, and excretion (ADME) studies were performed through oral, intraperitoneal and dermal exposures of radiolabeled ($^{14}C$) $C_{12}EO_3$ and $C_{12}EO_6$ (HERA 2009).

- *Absorption*: After oral and dermal exposures, $C_{12}EO_3$ and $C_{12}EO_6$ were completely absorbed (approximately 100%) (HERA 2009).
- *Distribution*: After oral and dermal exposures, $C_{12}EO_3$ and $C_{12}EO_6$ were minimally distributed to tissues (approx. 5%).
- *Metabolism*: Metabolism occurs via degradation of the ether linkage of the EO units and oxidation of the alkyl chain. Metabolism studies with radiolabeled AEs of varying alkyl chain and EO lengths found lower molecular weight PEG compounds which were ultimately broken down to $CO_2$ and water. Furthermore, with increased alkyl chain length, a higher percentage of $CO_2$ was produced.
- *Excretion*: After oral and dermal exposures, $C_{12}EO_3$ and $C_{12}EO_6$ were completely excreted (approx. 95%), mainly via urine; however, with increased EO length a higher proportion is excreted via feces and expired air. Furthermore, radiolabeled $CO_2$ were also found in the feces, with increased proportions correlating with increased ethoxylate chain length (HERA 2009).

In summary, AEs, such as dodecyl alcohol, ethoxylated (EO < 10), are readily absorbed via oral and dermal routes, minimally distributed to tissues (approx. 5%), and metabolized via degradation of the ether linkage of the EO units and oxidation of the alkyl chain into small MW PEG compounds and ultimately into $CO_2$. Rapid excretion (> 95%) occurred via urine, feces, and/or expired air $CO_2$.

**Hazard Classification Summary**

**Group I Human Health Effects (Group I Human)**

**Carcinogenicity (C) Score (H, M, or L): L**
Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Low for carcinogenicity based on a lack of carcinogenicity in long term studies. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate negative data are available and they are not GHS classified (CPA 2018b). Confidence in the score is high as the data are consistent and it is based on expert judgement by HERA.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- HERA 2009, AICIS 2019
  - *Oral: Surrogate: $C_{12\text{-}13}EO_{6.5}$*: In a 2-year dietary study in Sprague-Dawley rats (100/sex/dose), animals received $C_{12\text{-}13}EO_{6.5}$ in the diet at doses up to 1% (500 mg/kg/day). No increase in tumor incidence or other treatment-related pathologies were observed.
  - *Dermal: Surrogate: $C_{12\text{-}13}EO_{6.5}$*: In an 18-month dermal toxicity study in ICR Swiss mice, $C_{12\text{-}13}EO_{6.5}$ was applied to the back of the animals three times a week at 0, 0.2, or 5.0%. No treatment-related lesions were found. No further details were provided.
  - AEs are not carcinogenic based on lack of structural alerts to carcinogenicity, long term carcinogenicity studies, and reliable negative mutagenicity studies.
- OECD 2023
  - ToxServices evaluated dodecyl alcohol, ethoxylated (EO 1) using OECD Toolbox v.4.6 (OECD 2023); no structural alerts for genotoxic or nongenotoxic carcinogenicity were found (Appendix D).
- Based on the weight of evidence, a score of Low was assigned. $C_{12\text{-}13}EO_{6.5}$ has been tested in one oral and one dermal chronic carcinogenicity studies and have shown no evidence of carcinogenicity. Furthermore, no structural alerts for genotoxic or nongenotoxic carcinogenicity were identified for the target chemical.

**Mutagenicity/Genotoxicity (M) Score (H, M, or L): L**
Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Low for mutagenicity/genotoxicity based on Low for mutagenicity/genotoxicity based on negative results in a bacterial reverse mutation assay, *in vitro* mammalian cell mutagenicity assay, *in vitro* chromosome aberration assay and *in vivo* micronucleus assay for the target (EO 1-2.5). GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when negative data are available for both gene mutations and chromosome aberrations, and they are not GHS classified (CPA 2018b). The confidence in the score is high based on reliable data on the target compound along with expert judgement by HERA.

- 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 2023a
  - *In vitro*: In an Ames bacterial reverse mutation test (GLP unspecified), *Salmonella typhimurium* tester strains TA98, TA100, TA1535, and TA1537 were exposed to dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) in DMSO at 0, 1, 3, 10, 33, 100, 333, and 1,000 µg/plate with and without metabolic activation. The metabolic activation system consisted of 10% HLI (induced male Syrian hamster liver S9) and 10% RLI (induced

male Sprague Dawley rat liver S9). No information on precipitation was provided, and cytotoxicity was reported at the highest dose. Positive (i.e., sodium azide, 2-nitrofluorene, 9-aminoacridine, and 2-aminoanthracene (the authors of the ECHA dossier noted: "or occasionally, sterigmatocystin)) and negative controls were valid. No increase in the frequency of revertants was observed in any strain at any dose in the presence or absence of metabolic activation (Klimisch 2, reliable with restrictions).

- *In vitro*: In a chromosome aberration test (GLP unspecified), Chinese hamster ovary (CHO) cells were exposed to dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) in water up to 0, 5, 15, and 50 µg/mL with and without metabolic activation (Aroclor 1254 rat liver S9). Positive (i.e., mitomycin C and cyclophosphamide), and vehicle controls were reported as valid. No cytotoxicity or precipitation were observed, and the authors of the ECHA dossier note the highest concentrations tested were those yielding a sufficient number of suitable metaphase cells. No increase in the frequency of chromosome aberrations was detected with treatment in the presence or absence of metabolic activation (Klimisch 2, reliable with restrictions).
- *In vitro*: In a mammalian cell gene mutation assay (GLP unspecified), mouse lymphoma L5178Y cells were exposed to dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) in DMSO at up to 50 µg/mL with and without metabolic activation. The positive (methylmethanesulfonate and 3-methylcholanthrene) and vehicle controls were valid. No information was provided on precipitation or cytotoxicity. No increase in the mutation frequency was observed with treatment in the presence or absence of metabolic activation (Klimisch 2, reliable with restrictions).
- *In vivo*: In an *in vivo* micronucleus assay (GLP unspecified), male B6C3F1 mice (5/dose) were administered three doses of 0, 31.25, 62.5, or 125 mg/kg dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) in phosphate buffered saline (PBS) via gavage on three consecutive days, and were sacrificed after 24h (all doses) or 48h (control and high dose). Positive, negative, and vehicle controls were reported as valid. There were no increases in micronuclei in the bone marrow at any dose (Klimisch 2, reliable with restrictions).
- The authors of the ECHA dossier identified another study for *in vitro* genotoxicity; however, only the key studies were evaluated for this endpoint due to their higher reliability and more detailed information.

- HERA 2009
  - A large number of *in vivo* and *in vitro* mutagenicity and chromosomal aberration studies were conducted on AEs. None of them showed a potential for genotoxicity. These assays include negative bacterial reverse mutation assays, *in vitro* mammalian cell mutagenicity assays, *in vitro* chromosome aberration assays, and *in vivo* chromosome aberration assays. Most were performed according to GLP standards and OECD Guidelines and the remainder were well documented and conducted. It was concluded that AEs are not genotoxic.
- Based on the weight of evidence, a high confidence score of Low was assigned. There was no evidence of genetic toxicity in several well conducted *in vitro* and *in vivo* mutagenicity and chromosome aberration assays for dodecyl alcohol, ethoxylated (EO 1-2.5).

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

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Low for reproductive toxicity based on a NOAEL of 700 mg/kg/day, the highest dose tested, in a GLP-compliant, OECD Guideline 422 combined repeated dose toxicity study with the reproduction / developmental toxicity screening test with male and female Wistar rats exposed to dodecyl alcohol, ethoxylated (0-2 EO) supported by the absence of adverse reproductive effects in a two-generation reproductive toxicity study performed with

dodecyl alcohol, ethoxylated (EO 6), $C_{12}EO_6$. 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). Confidence in this score is high as it is based on reliable data on the target chemical.
Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2023a
    - A GLP-compliant combined repeated dose toxicity study with the reproduction / developmental toxicity screening test conducted according to OECD Guideline 422 was performed with male and female Wistar rats (10/sex/dose group main study, 5/sex/dose for recovery groups) administered oral doses of dodecyl alcohol, ethoxylated (0-2 EO, > 95% purity with ethylene oxide at an unspecified composition) in water at 0 (G1/G1R), 100 (G2), 300 (G3), and 700 (G4/G4R) mg/kg/day via gavage. Males were dosed for a total of 28 days, including two weeks prior to mating, during mating, and up to the day prior to sacrifice. Females were dosed for approximately 71 days covering two weeks prior to mating, during mating, during gestation, and until postnatal day 12. No adverse treatment related effects were reported on mortality, body weight, feed consumption, endocrine findings (T4 and TSH thyroid hormone measurements), gestation length, estrous cycle, sperm parameters, reproductive indices (male and female mating index, male and female fertility index, fecundity index, post-implantation loss), organ weights, gross pathology, and histopathology of reproductive organs. All animals in the top dose (G4) and top dose recovery groups (G4R) exhibited clinical signs of dullness from day 2 of treatment through to the end of treatment. The high dose recovery animals recovered with treatment removal. The mid- and high-dose animals exhibited higher precoital intervals; however, study authors considered these findings to be non-adverse due to a lack of corresponding effects on mating and fertility indices. Additionally, a dose-dependent increased in % post-implantation loss was reported in all treatment groups compared to the control group; however, % post implantation losses were less than 10% in all groups, and did not correspond with changes in any other reproductive/developmental parameter evaluated. The study authors identified a reproductive NOAEL of 700 mg/kg/day, the highest dose tested (Klimisch 1, reliable without restriction).
- HERA 2009
    - In a two-generation study, $C_{12}EO_6$ was given to rats (number and strain not specified) at dose levels of 25, 50 or 250 mg/kg/day. Three groups of animals received treatment continuously throughout the study while another three groups of females received the diet only during gestational day 6 – 15 while males were untreated. In addition to physical examinations, body weight, food consumption and mortalities, parameters related to reproductive toxicities were examined, including fertility, litter size, sex ratio, and pup viability and growth. On gestational day 13, representative females from each group of the FC generation (pups from the 3rd mating of the F0 and F1 parental generation) were sacrificed. The remaining females were sacrificed on gestational day 21. There were no treatment-related effects on general behavior, appearance, or survival of the parents or pups. The only effect observed was a reduced body weight gain of parental rats and pups at the highest dose. Therefore, Human & Environmental Risk Assessment (HERA) established the NOAEL for reproductive toxicity at 250 mg/kg/day.
    - Reproductive toxicity was not observed in a number of subchronic oral feeding studies that also examined reproductive organs.

**Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L):** *M*
Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Moderate for developmental toxicity based on decreased pup weight following exposure to the target chemical (EO 6), $C_{12}EO_6$, in the presence of maternal toxicity. GreenScreen® criteria classify chemicals as a Moderate hazard for developmental toxicity when there is limited or marginal evidence of developmental toxicity in animals (CPA 2018b). Confidence in the score was reduced due to uncertainty regarding the specificity of the measured effects.

- 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 2023a
  - *Oral:* In the previously described GLP-compliant combined repeated dose toxicity study with the reproduction / developmental toxicity screening test conducted according to OECD Guideline 422 was performed with male and female Wistar rats (10/sex/dose group main study, 5/sex/dose for recovery groups) administered oral doses of dodecyl alcohol, ethoxylated (0-2 EO, > 95% purity with ethylene oxide at an unspecified composition) in water at 0 (G1/G1R), 100 (G2), 300 (G3), and 700 (G4/G4R) mg/kg/day via gavage. Males were dosed for a total of 28 days, including two weeks prior to mating, during mating, and up to the day prior to sacrifice. Females were dosed for approximately 71 days covering two weeks prior to mating, during mating, during gestation, and until postnatal day 12. No adverse treatment related effects were reported on mortality, clinical signs of toxicity, body weight, food consumption, endocrine findings (T4 and TSH thyroid hormone measurements), the number and sex of pups, stillbirths, live births (live birth index), days 4 and 13 survival indices, pup weights, runts (pups significantly smaller than other pups), anogenital distance, nipple retention, histopathology, gross pathology, and presence of gross external abnormalities. Dose-dependent, treatment-related effects were reported for mid- and high-dose female pups including increased TSH and T4 levels; however, the study authors did not consider these findings adverse due to a lack of corresponding histopathology and gross pathology findings of the thyroid and parathyroid. The study authors identified a developmental NOAEL of 700 mg/kg/day, the highest dose tested (Klimisch 1, reliable without restriction).
- HERA 2009
  - *Oral:* In the previously described two-generation study, $C_{12}EO_6$ was given to rats (number and strain not specified) at dose levels of 25, 50 or 250 mg/kg/day. There were no treatment-related effects on general behavior, appearance, or survival of the parents or pups. The only effect observed was a reduced body weight gain of parental rats and pups at the highest dose. Therefore, a NOAEL and LOAEL of 50 and 250 mg/kg/day, respectively, for maternal and developmental toxicity, based on reduced body weight gain.
  - *Oral:* In a developmental toxicity study in rabbits, $C_{12}EO_6$ was administered to 25 pregnant rabbits orally at 0, 50, 100 or 200 mg/kg/day on gestational days 2 – 16. Animals were sacrificed on gestational day 28. Maternal toxicity was observed at 100 and 200 mg/kg/day in the form of ataxia and a slight decrease in body weight. Nine control animals and 31 treated animals died during the study (details not provided), and the surviving animals at the highest dose showed slight body weight reduction. Seven treated and two control animals had early deliveries. The NOAEL and LOAEL for developmental toxicity based on maternal toxicity were determined to be 50 and 100 mg/kg/day, respectively, according to HERA, with limited study details reported.
- AICIS 2019

  - *Dermal:* In two dermal studies in rats and rabbits exposed to $C_{12}EO_4$, developmental and teratogenicity NOAELs of > 240 - 300 mg/kg/day, respectively, were reported. No additional details were available.
- Based on the weight of evidence, a score of Moderate was assigned. No developmental effects were observed in a GLP-compliant, OECD Guideline 422 combined repeated dose toxicity study with the reproduction / developmental toxicity screening test with male and female Wistar rats exposed to dodecyl alcohol, ethoxylated (0-2 EO) with a developmental toxicity NOAEL of 700 mg/kg/day, the highest dose tested, even in the presence of maternal toxicity. However, reduced pup body weight was measured in oral studies with rats exposed to $C_{12}EO_6$ at maternally toxic doses, which may be nonspecific developmental effects due to maternal toxicity. Furthermore, developmental and teratogenicity NOAELs of > 240 - 300 mg/kg/day for rats and rabbits, respectively, exposed to $C_{12}EO_4$ were reported in two additional dermal studies (AICIS 2019). Therefore, ToxServices conservatively assigned a score of Moderate based on reduced pup body weight at maternally toxic oral doses for the target chemical (EO 6), $C_{12}EO_6$, in a two-generation toxicity study.

**Endocrine Activity (E) Score (H, M, or L):** DG
Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Data Gap for endocrine activity based on a lack of sufficient data identified for this endpoint. No endocrine effects (T4/TSH) were found in parents in an oral combined repeated dose toxicity study with reproductive and developmental toxicity screening test with the target compound (0-2 EO), and modeling did not identify any endocrine activity concerns. Adrenal, thyroid, and parathyroid weights were changed for high dose males, and dose-dependent increased TSH and T4 levels were reported for mid and high dose pups, without histopathological or gross pathological changes in the same oral combined repeated dose toxicity study with reproductive and developmental toxicity screening for the target chemical (0-2 EO). Due to insufficient *in vivo* data for all relevant endocrine pathways (i.e., estrogen agonism and antagonism, androgen agonism and antagonism, thyroid, and steroidogenesis), a Data Gap was assigned.

- 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 2023a
  - *Oral:* In the previously described GLP-compliant combined repeated dose toxicity study with the reproduction / developmental toxicity screening test conducted according to OECD Guideline 422 was performed with male and female Wistar rats (10/sex/dose group main study, 5/sex/dose for recovery groups) administered oral doses of dodecyl alcohol, ethoxylated (0-2 EO, > 95% purity with ethylene oxide at an unspecified composition) in water at 0 (G1/G1R), 100 (G2), 300 (G3), and 700 (G4/G4R) mg/kg/day via gavage. Males were dosed for a total of 28 days, including two weeks prior to mating, during mating, and up to the day prior to sacrifice. Females were dosed for approximately 71 days covering two weeks prior to mating, during mating, during gestation, and until postnatal day 12. No adverse treatment related effects were reported on mortality, clinical signs of toxicity, body weight, food consumption, endocrine findings (T4 and TSH thyroid hormone measurements), the number and sex of pups, stillbirths, live births (live birth index), days 4 and 13 survival indices, pup weights, runts (pups significantly smaller than other pups), anogenital distance, nipple retention, histopathology, gross pathology, and presence of gross external abnormalities. For top-dose males, decreased absolute adrenal weight, increased absolute thyroid and parathyroid weight, and increase in testes weight were reported; however, these findings were not considered to be adverse due to a lack of correlating histopathology and gross pathology. Dose-dependent, treatment-related effects were

reported for mid- and high-dose female pups including increased TSH and T4 levels; however, the study authors did not consider these findings adverse due to a lack of corresponding histopathology and gross pathology findings of the thyroid. The study authors identified a reproductive and developmental NOAEL of 700 mg/kg/day, the highest dose tested (Klimisch 1, reliable without restriction).

- U.S. EPA 2023b
  - Dodecyl alcohol, ethoxylated (EO < 10) was not evaluated as part of the U.S. EPA's Endocrine Disruptor Screening Program (EDSP) in the 21st Century; however, the ToxCast CERAPP Potency Level model predicted dodecyl alcohol, ethoxylated (EO < 10) was inactive for estrogen receptor agonist, antagonist, and binding (Appendix E).
- DTU 2023
  - Modeling in the Danish QSAR database provides the following results that are within the applicability domains of the models (Appendix F):
    - Dodecyl alcohol, ethoxylated (EO < 10) is predicted to be negative for estrogen receptor α binding (full training set, human *in vitro*) by the CaseUltra model;
    - Dodecyl alcohol, ethoxylated (EO < 10) is predicted to be negative for estrogen receptor α binding (balanced training set, human *in vitro*) by the model battery consisting of negative and in domain predictions by the CaseUltra and SciQSAR models;
    - Dodecyl alcohol, ethoxylated (EO < 10) is predicted to be negative for estrogen receptor α activation (human *in vitro*) by the CaseUltra model, and positive by the SciQSAR model;
    - Dodecyl alcohol, ethoxylated (EO < 10) is predicted to be negative for androgen receptor inhibition (human *in vitro*) by the model battery consisting of negative and in domain predictions by the CaseUltra and Leadscope models;
    - Dodecyl alcohol, ethoxylated (EO < 10) is predicted to be negative for estrogen receptor activation (CERAPP data *in vitro*) and for androgen receptor binding, inhibition and activation (CoMPARA data *in vitro*) and thyroperoxidase (TPO) inhibition (QSAR1 and QSAR2, rat *in vitro*) by the Leadscope models.

**<u>Group II and II* Human Health Effects (Group II and II* Human)</u>**

***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): M**

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Moderate for acute toxicity based on oral $LD_{50}$ values as low as 1,000 mg/kg. GreenScreen® criteria classify chemicals as a Moderate hazard for acute toxicity when oral $LD_{50}$ values are between 300 and 2,000 mg/kg (CPA 2018b). Confidence in the score is high because it is based on measured data on the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - GHS – New Zealand – Acute oral toxicity – Category 4.
      - Based on an oral $LD_{50}$ of 384 mg/kg in guinea pigs (CCID 2023).
    - GHS – Japan – H302 – Harmful if swallowed [Acute toxicity (oral) – Category 4].
      - No information was provided for the basis of classification (NITE Undated, 2021).

    - GHS – Australia – H302 – Harmful if swallowed [Acute toxicity (oral) – Category 4].
- ECHA 2023a
    - *Oral:* Dodecyl alcohol, ethoxylated (EO 1-2.5): $LD_{50}$ (female Wistar rat) = 1,000 mg/kg (GLP-compliant, OECD Guideline 423) (Klimisch 1, reliable without restriction).
    - *Oral:* Dodecyl alcohol, ethoxylated (EO 1-2.5): $LD_{50}$ (rat, sex and species unspecified) = 1,190 mg/kg (GLP-unspecified) (Klimisch 2, reliable with restrictions).
    - *Oral:* Dodecyl alcohol, ethoxylated (EO 1-2.5): $LD_{50}$ (rat, sex and species unspecified) = 1,000 mg/kg (GLP-unspecified) (Klimisch 2, reliable with restrictions).
    - *Oral:* Dodecyl alcohol, ethoxylated (EO 1-2.5): $LD_{50}$ (mouse, sex and species unspecified) = 1,170 mg/kg (GLP-unspecified) (Klimisch 2, reliable with restrictions).
    - *Dermal:* Dodecyl alcohol, ethoxylated (EO 1-2.5): $LD_{50}$ (male and female Wistar rat) > 2,000 mg/kg (GLP-compliant, OECD Guideline 402) (Klimisch 1, reliable without restriction).
    - *Dermal:* Dodecyl alcohol, ethoxylated (EO 1-2.5): $LD_{50}$ (male and female Wistar rat) > 2,000 mg/kg (non-GLP-compliant, OECD Guideline 402) (Klimisch 2, reliable with restrictions).
- HERA 2009
    - In general, the acute toxicity of AEs across all routes of exposure was not meaningfully affected by the length of the alkyl chain. Only acute oral toxicity was affected by the number of EO units.
    - *Oral*: Acute oral toxicity of AEs is dependent on the number of EO units in a parabolic fashion but does not depend on the length of the alkyl chain. AEs with EO units of greater than 5 and less than 14 have higher acute oral toxicity relative to AEs with EO units less than 4 or more than 21. Acute oral toxicity is similar between linear and branched AEs.
    - *Oral:* The acute toxicity of AEs is associated with the number of EO units rather than the carbon chain lengths.
        - $C_xEO_{1-3}$: $LD_{50}$ = 4,000 mg/kg to > 10,000 mg/kg
        - $C_xEO_{4-6}$: $LD_{50}$ = 1,200 mg/kg to > 10,000 mg/kg
        - $C_xEO_{7-9}$: $LD_{50}$ = 1,100 mg/kg to 3,400 mg/kg
    - *Inhalation:* Data on acute inhalation studies are scarce for AEs. With available data, it was concluded that they have low acute inhalation toxicity in rats with $LD_{50}$ values exceeding the saturated vapor concentration in air. Acute toxic thresholds were reached only when exposed to undiluted chemicals in respirable mist or aerosol forms.
        - *Surrogate: $C_{9-11}EO_5$*: 4h $LC_{50}$ (mist) > 0.22 mg/L.
    - *Dermal:* There is no relationship between alkyl chain length or number of EO units and acute dermal toxicity.
    - *Dermal:* In rabbits dermal $LD_{50}$ values were determined to be in the range of greater than 2,000 to 5,200 mg/kg. On the basis of these results, AEs can be considered to be slightly to practically non-toxic by the dermal route of application.
        - *Surrogate: $C_{9-11}EO_x$*: > 2,000 mg/kg to > 4,000 mg/kg

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

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Moderate for systemic toxicity (single dose) based on a potential of respiratory irritation reactions. Respiratory tract irritation classifies chemicals as GHS Category 3 specific target organ toxicants following single exposure for respiratory irritation. 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 exposure for respiratory irritation (H335 – May cause respiratory irritation) (CPA 2018b). Confidence in this score is reduced as limited data are available for respiratory irritation.

- 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 2023a
  - *Oral:* In the previously described GLP-compliant acute oral toxicity study conducted according to OECD Guideline 423 that reported an $LD_{50}$ value of 1,000 mg/kg, females Wistar rats were administered single oral doses of 300 or 2,000 mg/kg (n=6 and 3, respectively) dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) in water and observed up to 14 days. Two out of three animals of the high dose group died on day 1 post-exposure with the third animals surviving through to the end of the study period. External gross pathological findings for the deceased high dose animals included soiled anal region and internal gross pathological findings included moderate to severe red discoloration of all lobes of the lungs. Due to the high mortality in the 2,000 mg/kg groups, six additional animals were treated with 300 mg/kg test substance and no mortalities were reported. The surviving high dose animal exhibited clinical signs of toxicity post-dosing including diarrhea up to 1 hour, mild lethargy at 1 to 4 hours, soiled anal region with feces and urine at 1 to 3 hours, epistaxis (nosebleeds) at 3 hours, and soiled anal region with urine up to 6 hours post-dosing; however, there were no treatment related clinical signs reported for the 300 mg/kg group. Furthermore, for the surviving animals (1/3- high dose, 6/6 - low dose), no effects were reported on body weight gain, or internal and external gross pathology (Klimisch 1, reliable without restriction).
    - Limited information was provided for the remaining oral acute toxicity studies identified by the authors of the ECHA dossier; therefore, only the key, GLP-compliant, guideline study was used to evaluate the oral route of exposure for this endpoint due to its higher reliability.
  - *Dermal:* In the previously described GLP-compliant dermal acute toxicity study conducted according to OECD Guideline 402 that reported an $LD_{50}$ value > 2,000 mg/kg, male and female Wistar rat (5/sex) were administered topical applications of 2,000 mg/kg undiluted dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, 99.28% active ingredient (a.i.) content) for 24 hours under occlusive conditions and followed by a 14-day observation period. No treatment related effects on mortality, clinical signs of toxicity, or gross pathology at necropsy were reported (Klimisch 1, reliable without restriction).
  - *Dermal:* In the previously described non-GLP-compliant dermal acute toxicity study conducted according to OECD Guideline 402 that reported an $LD_{50}$ value > 2,000 mg/kg, male and female Wistar rat (5/sex/group) were administered topical applications of 2,000 mg/kg dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) in water for 24 hours under occlusive conditions and followed by a 14-day observation period. No treatment related effects on mortality, clinical signs of toxicity, or adverse gross pathology findings at necropsy were reported (Klimisch 2, reliable with restrictions).
- AICIS 2019
  - In Australian Industrial Chemicals Introduction Scheme (AICIS)'s evaluation of ethoxylates of aliphatic alcohols (> C6), respiratory irritation was identified as a hazard concern due to the inhalation of aerosolized products causing respiratory irritation and damage to the lung with prolonged or repeated exposure.

- HERA 2009
    - *Inhalation:* The respiratory tract irritation potential is not concerning due to the expected low exposure to aerosolized AEs during the use of household cleaning products. *ToxServices noted that a GreenScreen® assessment is a hazard assessment and does not consider exposure potential.*
- Based on the weight of evidence, a score of Moderate was assigned. In the GLP-compliant, OECD Guideline 423 study in rats exposed to the target chemical, increased mortalities with clinical signs of toxicity prior to death and moderate to severe red discoloration of all lobes of the lungs were reported for 2/3 high dose animals at 1,000 mg/kg; however, there were no treatment related effects reported for low dose animals at 300 mg/kg including mortalities, clinical signs of systemic toxicity, body weight gains, and internal/external gross pathology findings. Additionally, there were no treatment related systemic toxicity observed in acute dermal toxicity studies with the target chemical. Therefore, the target chemical is not classified as GHS Category 1 or 2 specific target organ toxicants following single exposures (UN 2021). However, the irritating properties to the skin and eyes (see relevant sections below) suggest that concentrated AEs may be irritating to the respiratory tract as well. This classifies the target chemical as a GHS Category 3 specific target organ toxicant following single exposures for respiratory irritation.

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

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Low for systemic toxicity (repeated dose) based on the lack of adverse systemic toxicity in oral and dermal repeated dose toxicity studies in animals exposed to the target chemical and/or surrogate AEs. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when adequate data are available and they are not classified according to GHS (CPA 2018b). Confidence in the score is high as it is based on experimental data from well conducted studies on the target chemical 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 2023a
    - *Oral:* In the previously described GLP-compliant combined repeated dose toxicity study with the reproduction / developmental toxicity screening test conducted according to OECD Guideline 422 was performed with male and female Wistar rats (10/sex/dose group main study, 5/sex/dose for recovery groups) administered oral doses of dodecyl alcohol, ethoxylated (0-2 EO, > 95% purity with ethylene oxide at an unspecified composition) in water at 0 (G1/G1R), 100 (G2), 300 (G3), and 700 (G4/G4R) mg/kg/day via gavage. Males were dosed for a total of 28 days, including two weeks prior to mating, during mating, and up to the day prior to sacrifice. Females were dosed for approximately 71 days covering two weeks prior to mating, during mating, during gestation, and until postnatal day 12. There were no adverse treatment-related effects reported on mortality, clinical signs of toxicity (low and mid dose only), body weight/weight gain, food consumption, hormone analysis (thyroid: T4, TSH), hematology, clinical chemistry, absolute and relative organ weights, gross pathology, and histopathology. Effects related to neurotoxicity are discussed in the neurotoxicity section below. Study authors identified NOAELs and LOAELs based on neurotoxicity (Klimisch 1, reliable without restriction). *As there are no effects other than neurotoxicity, ToxServices identified a NOAEL of 700 mg/kg/day for systemic toxicity (excluding neurotoxicity) for this endpoint. As the duration of exposure in the above study was less than 90 days, ToxServices adjusted the GHS guidance values of 10 and 100*

*mg/kg/day (UN 2021) by a factor of 3 (28 days are roughly one third of 90 days) to 30 and 300 mg/kg/day for males and a factor of 1.25 (90/72) to 12.5 and 125 mg/kg/day for females. The NOAEL of 700 mg/kg/day are above the adjusted guidance values of 125 and 300 mg/kg/day; therefore, ToxServices did not classify dodecyl alcohol, ethoxylated (0-2 EO) as a repeated dose systemic toxicant under GHS criteria (UN 2021).*

- HERA 2009
  - *Oral: Surrogate: $C_{12-15}$ $EO_7$ and $C_{12-14}$ $EO_7$:* Subchronic dietary feeding studies were conducted win male and female Wistar rats that were administered diets containing $C_{12-15}EO_7$ or $C_{12-14}EO_7$ at concentrations of 0, 0.0313, 0.0625, 0.125, 0.25, 0.5, or 1.0% for 90 days. In both studies, body weight gain was significantly reduced in both sexes at doses greater than 0.25% and corresponded to reduced food and water intake. Relative liver weights were significantly increased in males at 0.5% and above and in females at 0.25% and above. Histopathology showed evidence of hepatocytic enlargement indicative of increased liver metabolism. Authors identified a NOAEL of 0.125% based on effects on liver pathology, and report that this concentration is equivalent to 102 mg/kg/day for $C_{12-15}EO_7$ and 110 mg/kg/day for $C_{12-14}EO_7$.
  - *Oral: Surrogate: $C_{12-14}EO_7$*: A series of oral feeding studies were performed in the same lab with Colworth-Wistar rats (60/group) provided diets containing $C_{12-14}EO_7$ (linear), $C_{16-18}EO_{18}$ (linear), or $C_{12-15}EO_{3-11}$ (branched) at 0.023-1.5% for 21 days. The principally affected organ was the liver based on increased liver weights and hepatic hypertrophy. The NOAELs were in the narrow range of 433-519 mg/kg/day, indicating a lack of correlation between the repeated oral dose toxicity and length of alkyl chain, degree of branching, or number of EO units.
  - *Dermal: Surrogate: $C_{9-11}$ $EO_6$:* A GLP-compliant 90-day dermal toxicity study was conducted in rats according to OECD Guideline 411. Animals (10/sex/dose) were exposed to 1, 10 or 25% test substance; equivalent to 8, 80 and 200 mg/kg/day, respectively, according to HERA. Clinical observations, urine and blood analyses and histopathology were performed. No signs of irritation were found at the application site, but dry and flaky skin was noted at 10 and 25%. There was an increase in relative kidney weights in both sexes without pathological findings. The NOAEL was established at 10% (80 mg/kg/day) based on kidney weight increase (LOAEL = 200 mg/kg/day). *However, ToxServices does not consider the increased kidney weights without correlating changes to renal histopathology to be sufficient for determination of a LOAEL for systemic toxicity. Therefore, ToxServices identified a NOAEL of 200 mg/kg/day based on the lack of significant systemic toxicity at the highest dose level tested in this study.*
- Based on the weight of evidence, a score of Low was assigned. In a GLP-compliant OCED Guideline 422 study in rats exposed to the target chemical, a systemic toxicity NOAEL of 700 mg/kg/day is above the duration-adjusted guidance values for Category 2 (UN 2021). Furthermore, the available oral and dermal subchronic repeated dose toxicity studies with the several similar AEs showed a lack of adverse effects at and above the guidance values of 100 mg/kg/day and 200 mg/kg/day, respectively, for a 90-day study. Based on this weight of evidence, dodecyl alcohol, ethoxylated (< 10 EO) was not classified as a systemic toxicant after repeated exposure under GHS criteria (UN 2021).

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

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Low for neurotoxicity (single dose) based on lack of clinical signs and gross pathology findings indicative of specific neurotoxicity at non-lethal doses in acute oral and dermal studies. GreenScreen® criteria classify chemicals as a Low hazard

for neurotoxicity (single dose) when adequate data are available and they are not classified under GHS (CPA 2018b). The confidence in the score is low as the acute toxicity studies did not perform comprehensive neurobehavioral exams.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - GHS – Japan – H336 – May cause drowsiness or dizziness [Specific target organ toxicity – Single exposure – Category 3 (Narcotic effects)].
      - No information was provided for the basis of classification (NITE Undated, 2021).
- ECHA 2023a
  - *Oral:* In the previously described, GLP-compliant acute oral toxicity study conducted according to OECD Guideline 423 that reported an $LD_{50}$ value of 1,000 mg/kg, females Wistar rats were administered single oral doses of 300 or 2,000 mg/kg (n=6 and 3, respectively) dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) in water and observed up to 14 days. Two out of three animals of the high dose group died on day 1 post-exposure with the third animals surviving through to the end of the study period. External gross pathological findings for the deceased high dose animals included soiled anal region and internal gross pathological findings included moderate to severe red discoloration of all lobes of the lungs. The surviving high dose animal exhibited clinical signs of toxicity post-dosing including diarrhea up to 1 hour, mild lethargy at 1 to 4 hours, soiled anal region with feces and urine at 1 to 3 hours, epistaxis (nosebleeds) occurred at 3 hours, and soiled anal region with urine up to 6 hours post-dosing. Due to the high rate of deaths in the 2,000 mg/kg groups, six additional animals were treated with 300 mg/kg test substance and no mortalities were reported. Furthermore, for the surviving animals (1/3- high dose, 6/6 - low dose), no effects were reported on body weight gain, clinical signs of toxicity, or internal and external gross pathology findings (Klimisch 1, reliable without restriction).
    - Limited information was provided for the remaining oral acute toxicity studies identified by the authors of the ECHA dossier; therefore, only the key, GLP-compliant, guideline study was used to evaluate the oral route of exposure for this endpoint due to its higher reliability.
  - *Dermal:* In the previously described GLP-compliant dermal acute toxicity study conducted according to OECD Guideline 402 that reported an $LD_{50}$ value > 2,000 mg/kg, male and female Wistar rat (5/sex) were administered topical applications of 2,000 mg/kg undiluted dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, 99.28% a.i. content) for 24 hours under occlusive conditions and followed by a 14-day observation period. No treatment related effects on mortality, clinical signs of toxicity, or gross pathology findings at necropsy were reported (Klimisch 1, reliable without restriction).
  - *Dermal:* In the previously described non-GLP-compliant dermal acute toxicity study conducted according to OECD Guideline 402 that reported an $LD_{50}$ value > 2,000 mg/kg, male and female Wistar rat (5/sex/group) were administered topical applications of 2,000 mg/kg dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) in water for 24 hours under occlusive conditions and followed by a 14-day observation period. No treatment related effects on mortality, clinical signs of toxicity, or adverse gross pathology findings at necropsy were reported (Klimisch 2, reliable with restrictions).
- Based on the weight of evidence, a score of Low was assigned. While clinical signs of neurotoxicity (i.e., mild lethargy) were reported for the one surviving high dose, 1,000 mg/kg, animal (1/3), no clinical signs of neurotoxicity or internal/external gross pathology findings, including evaluation of

the brain and spinal cord, were reported for remaining 6 low dose, 300 mg/kg, animals. In addition, 1,000 mg/kg was a dose that caused lethality. Additionally, no treatment related signs of neurotoxicity were reported in two acute dermal toxicity studies with the target chemical.

**Neurotoxicity (repeated dose, N-repeated) (Group II*) Score (H, M, or L):** *M*
Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Moderate for neurotoxicity (repeated dose) based on a male LOAEL of 300 mg/kg/day, which is equal to the duration-adjusted GHS Category 2 guidance values of 300 mg/kg/day, in a GLP-compliant OECD Guideline 422 combined repeated dose toxicity study with the reproduction / developmental toxicity screening test with neurobehavioral examination in rats exposed to the target chemical. GreenScreen® criteria classify chemicals as a Moderate hazard for neurotoxicity (repeated dose) when they are classified to GHS Category 2 (CPA 2018b). Confidence in the score is low as the critical effects, reduced locomotor activity, was reversible after a recovery period, leading to its unclear toxicological significance.

- 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 2023a
  - *Oral:* In the previously described GLP-compliant combined repeated dose toxicity study with the reproduction / developmental toxicity screening test conducted according to OECD Guideline 422 was performed with male and female Wistar rats (10/sex/dose group main study, 5/sex/dose for recovery groups) administered oral doses of dodecyl alcohol, ethoxylated (0-2 EO, > 95% purity with ethylene oxide at an unspecified composition) in water at 0 (G1/G1R), 100 (G2), 300 (G3), and 700 (G4/G4R) mg/kg/day via gavage. Males were dosed for a total of 28 days, including two weeks prior to mating, during mating, and up to the day prior to sacrifice. Females were dosed for approximately 71 days covering two weeks prior to mating, during mating, during gestation, and until postnatal day 12. There were no adverse treatment-related effects reported on mortality, clinical signs of toxicity (low and mid dose only), absolute and relative organ weights, gross pathology, and histopathology. All animals in the top dose (G4) and top dose recovery groups (G4R) exhibited clinical signs of dullness from day 2 of treatment through to the end of treatment. The high dose recovery animals recovered with treatment removal. For mid dose males, a dose-dependent and statistically significant decrease in fore- and hind limb grip strengths was reported as well as decreases in locomotor activity for both mid and high dose males. The remaining parameters evaluated in the functional observation battery (FOB) were unremarkable in males, and no adverse treatment related effects were reported for females in any treatment group. Furthermore, locomotor activity completely reversed during the recovery period for all high dose recovery (G4R) animals. Study authors identified a female systemic toxicity NOAEL and LOAEL of 300 and 700 mg/kg/day, respectively, based on clinical signs of dullness in all female rats throughout the study observed at 700 mg/kg/day, the highest dose tested, and a male systemic toxicity NOAEL and LOAEL of 100 and 300 mg/kg, respectively, based on a dose-dependent decrease in locomotor activity at doses at and above 300 mg/kg/day (Klimisch 1, reliable without restriction). *As the duration of exposure in the above study was less than 90 days, ToxServices modified the GHS guidance values of 10 and 100 mg/kg/day (UN 2021) by a factor of 3 (28 days are roughly one third of 90 days) to 30 and 300 mg/kg/day for males. The LOAEL of 300 mg/kg/day for males is equal to the adjusted guidance values of 300 mg/kg/day; thereby warranting classification to GHS Category 2 (UN 2021).*

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

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Low for skin sensitization based on the lack of dermal sensitization reactions in animal and human studies for the target chemical (EO 1-2.5). GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data are available and negative and they are not GHS classified (CPA 2018b). Confidence in the score is high as it is based on reliable data on the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2023a
  - In a non-GLP-compliant Draize test, male guinea pigs (7/group, species unspecified) received during induction a series of 10 intradermal injections containing a 0.02% or 0.1% solution of an aerosol formulation of dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) in water every other day, three times a week for 3 weeks. During challenge, animals received a single intradermal injection containing 0.05 mL test substance in water. No direct and delayed sensitization reactions were reported for any treatment group. The study authors concluded the test substance was a non-skin sensitizer under the conditions of this test (Klimisch 2, reliable with restrictions).
  - In a Draize skin sensitization test, albino rabbits (12/group, sex unspecified) received topical applications 5 mL of 1% dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity and vehicle listed as "solution" without further information) to intact and abraded skin under occlusive conditions for 10 days during induction and for 48 hours during challenge. Slight erythema irritation was reported without a difference between intact or abraded skin; however, no positive sensitization reactions were reported in any treatment group. Therefore, the study authors concluded the test substance was non-sensitizing under the conditions of this study (Klimisch 2, reliable with restrictions).
  - In a human repeated insult patch test (HRIPT), male and female volunteers received during induction three weekly topical applications of 10, 15, and 20% of dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) in aerosol creams (noted as contraceptive creams) under occlusive conditions for 3 weeks during induction (53 subjects: 13 males, 40 females) and a single topical application under occlusion for 72 hours during challenge (51 subjects: 12 males and 39 females). Mild erythema irritation without edema was reported with increased incidence occurring with increased applications; however, no sensitization reactions were reported in any treatment group; therefore, the study authors concluded the test substance was non-sensitizing under the conditions of this study (Klimisch 2, reliable with restrictions).

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

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Low for respiratory sensitization based on a lack of dermal sensitization potential and according to ECHA's guidance on respiratory sensitization evaluation. GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when adequate and negative data and no GHS classification are available (CPA 2018b). Confidence in the score was low as this evaluation did not include non-immunologic mechanisms of respiratory sensitization, and no specific data were available for respiratory sensitization.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2023

  - Dodecyl alcohol, ethoxylated (EO 1) does not contain any structural alerts for respiratory sensitization (Appendix D).
- DTU 2023
  - Dodecyl alcohol, ethoxylated (EO < 10) is predicted to be negative for respiratory sensitization in humans by the model battery consisting of negative and in domain predictions by the Leadscope and SciQSAR models. The predictions from the remaining models were outside their applicability domains (Appendix G).
- 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 dodecyl alcohol, ethoxylated (EO < 10) 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 the target chemical, and as it does not contain any structural alerts for respiratory sensitization (OECD 2023), dodecyl alcohol, ethoxylated (EO < 10) is not expected to be a respiratory sensitizer.

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

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Low for skin irritation/corrosivity based on the lack of dermal irritation detected in two OECD Guideline 404 studies in rabbits exposed to neat target chemical (EO 1-2.5). AEs with higher EO numbers are less irritating to the skin. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate and negative data and no GHS classification are available (CPA 2018b). The confidence in the score was high as it was based on reliable, high quality measured data on the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - GHS – Australia – H315 – Causes skin irritation [Skin corrosion/irritation – Category 2].
- ECHA 2023a
  - A GLP-compliant skin irritation test conducted according to OECD Guideline 404 was performed with three New Zealand White rabbits (sex unspecified) administered topical applications of undiluted dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, 99.28% a.i. content) to clipped skin under semi-occlusive conditions for 4 hours. An observation period of up to 72 hours followed the exposure period. At 24, 48, and 72 hours, the individual erythema and edema scores for animals 1, 2, and 3 were 0. No skin irritation was reported at any treated site during the study. The study authors concluded that dodecyl alcohol, ethoxylated (1 - 2.5 mol EO) was not irritating to the skin in this study (Klimisch 1, reliable without restriction).
  - A non-GLP-compliant skin irritation test conducted according to OECD Guideline 404 was performed with three female New Zealand White rabbits administered topical applications of 0.5 mL undiluted dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) to clipped, intact skin under occlusive conditions for 4 hours. An observation period of up to 14 days followed the exposure period. The mean primary dermal irritation index (PDII) at 24 hours was 0.92. At 24 hours, slight erythema was reported in all three animals with individual scores for erythema at 24 hours of 1. This irritation was fully reversible by 48

hours as there was no indication of irritation at 48 or 72 hours, or after 14 days. The study authors concluded that dodecyl alcohol, ethoxylated (1 - 2.5 mol EO) was not irritating to the skin in this study (Klimisch 2, reliable with restrictions).
    - In a GLP-compliant *in vitro* reconstructed human epidermis test conducted according to OECD Test Guideline 439, MatTek EpiDerm™ tissue samples were treated with 30 µL neat dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) for 60 minutes and then incubated with MTT solution for 42 hours. Aliquots of MTT solution were then used to evaluate tissue viability via spectrophotometry. The positive, 5% SDS, and negative controls were valid. The mean % tissue viability compared to the negative control was 2.7% for the test substance; therefore, the test substance was considered to be irritating to the skin under the conditions of the test (Klimisch 1, reliable without restriction). *A test substance that is predicted as irritating to the skin in an OECD Test Guideline 439 RhE test can be classified as "not classified" or "irritating to the skin in Category 2"; therefore, would require additional testing to rule out a Category 2 classification (OECD 2014). Classification is not possible based on the results of this study alone.*
- HERA 2009
    - AEs with a lower degree of ethoxylation (i.e., 1-3) are more irritating than those with a higher degree of ethoxylation (>4). AEs are less irritating to human skin than to animal skin
- CETOX 2001
    - The skin irritating potential of AEs generally decreases with increasing level of ethoxylation.
- In summary, undiluted dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) was non-irritating in two OECD Guideline 404 studies in rabbits. HERA (2009) reports that AEs with a lower degree of ethoxylation (i.e., 1-3) are more irritating than those with a higher degree of ethoxylation. Therefore, dodecyl alcohol, ethoxylated with higher number of EOs (EO 3-9) are not likely to be more irritating than the tested dodecyl alcohols, ethoxylated (1-2.5 EO). Based on this weight of evidence, ToxServices assigned a Low score.

**Eye Irritation/Corrosivity (IrE) (Group II) Score (vH, H, M, or L):** *H*
Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of High based on ToxServices classifying it to GHS Category 2A. GreenScreen® criteria classify chemicals as a High hazard for eye irritation/corrosivity when they are classified to GHS Category 2A (CPA 2018b). Confidence in the score is reduced as the results from the high quality *in vivo* study does not quite meet GHS classification criteria, and another *in vitro* study does not support classification, either.
- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:*
        - GHS – New Zealand – Serious eye damage category 1.
            - Based on severe eye irritation in rabbits (CCID 2023).
        - GHS – Australia – H318 – Causes serious eye damage [Serious eye damage/eye irritation – Category 1].
            - Based on a category assessment for ethoxylates of aliphatic alcohols (C > 6) (AICIS 2019).
- ECHA 2023a
    - A GLP-compliant ocular irritation test conducted according to OECD Guideline 405 was performed with three female New Zealand White rabbit administered an ocular instillation of 0.1 mL undiluted dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, 99.28% a.i. content) and observed up to 24 hours. The eye irritation was evaluated via the Draize method. The mean corneal opacity and iris scores across 24, 48, and 72 hours for animals 1, 2, and 3 were 0.

The mean conjunctiva scores across 24, 48, and 72 hours for animals 1, 2, and 3 were 1.67, 1.67, and 2, respectively. The mean chemosis scores across 24, 48, and 72 hours for animals 1, 2, and 3 were 1, 1.33, and 1, respectively. All irritative effects were fully resolved within the 14-day observation period. The study authors concluded that the test substance was irritating to the eye in this study and classified it as a Category 2 eye irritant (Klimisch 1, reliable without restriction). *ToxServices notes irritation effects were not fully reversed by Day 7. However, based on the GHS criteria which classifies a chemical as an ocular irritant when mean scores are at 2 for conjunctival redness and/or chemosis in 2/3 animals following gradings at 24, 48, and 72 hours, dodecyl alcohol, ethoxylated (1 - 2.5 mol EO) does not meet classification criteria for Categories 2A/2B (UN 2021).*

- In a non-GLP-compliant *in vitro* reconstructed human cornea-like epithelium test conducted according to OECD Test Guideline 492, EpiOcular™ tissue samples were treated with 50 µL unchanged (no vehicle) dodecyl alcohol, ethoxylated (1 - 2.5 mol EO, purity unspecified) for approximately 30 minutes. After treatment, treated tissues were rinsed and then incubated with the MTT solution. Aliquots of MTT solution were then used to evaluate tissue viability via spectrophotometry. The mean % tissue viability was determined to be 34.4%, therefore, the test substance was considered to be irritating to the eyes of humans under the conditions of the test and classified as a Category 2 eye irritant (Klimisch 1, reliable without restriction). *A test substance that is predicted to be irritating to the eye in an OECD Test Guideline 492 test requires additional testing to differentiate between GHS Category 1 and Category 2, and between Category 2A and 2B (OECD 2019). In this case, additional data are required to differentiate between Category 2A and 2B.*
- A bovine corneal opacity and permeability (BCOP) test (GLP-unspecified) conducted according to the method of Muir (1984/1985) was performed with bovine eyes (15 corneas per treatment group, 3 corneas per control) exposed to 0.75 mL of dodecyl alcohol, ethoxylated (1-3 EO, purity unspecified) in 10% minimum essential medium (MEM) for 10 minutes at 32°C with a post-incubation at 32°C for 120 minutes. The mean *in vitro* irritation score (IVIS) was 0.1. Vehicle and negative controls were valid (Klimisch 2, reliable with restrictions). *As the irritation score was ≤ 3, the test substance was not irritating and not classified under GHS criteria for eye irritants (OECD 2019, UN 2021).*
- Eight supporting studies are available on dodecyl alcohol. Ethoxylated (EO 1-2.5) in the REACH registration dossier, reporting no irritation to moderate irritation. However, the studies either tested the diluted compound, or used protocols resulting in irritation scores not directly comparable to GHS criteria. Therefore, ToxServices did not include these studies in this assessment. The ECHA dossier authors classified dodecyl alcohol, ethoxylated (1-2.5 EO) to GHS Category 2 for eye irritation based on the overall weight of evidence. ToxServices notes that in the European Union, Category 2B classification is not adopted. Therefore, Category 2 under CLP is equivalent to Category 2A under GHS.

- Based on the weight of evidence, a score of High was assigned. Mild to moderate irritation was reported in an OECD Guideline 404 study in rabbits, an *in vitro* OECD Guideline 492 study in human cells, and a BCOP test exposed to the dodecyl alcohol, ethoxylated (< 3 EO). Of the three studies available, only one *in vitro* study suggests an eye irritation potential (Category 2A/2B). Results from the *in vivo* study is slightly under the GHS Category 2A classification criteria (conjunctival redness scores of (1.67, 1.67 and 2 in three animals, vs 2 of 3 animals with scores ≥ 2), with effects being reversible in 21 days, but not 7 days. ToxServices conservatively classified dodecyl alcohol, ethoxylated (EO < 10), which is consistent with the classification made by the ECHA dossier authors. Although no information is available for the degree of eye irritation expected for dodecyl alcohol, ethoxylated (4 - < 9 EO), skin irritation studies suggest that the

irritation potential decreases as the EO number increases. The GHS Category 1 classifications made by Australia is based on data on the chemical class, and the basis for New Zealand's Category 1 classification is not sufficiently detailed. Therefore, ToxServices did not put much weight on these classifications.

## Ecotoxicity (Ecotox)

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

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of High for acute aquatic toxicity based on acute aquatic toxicity values as low as 1.225 mg/L in algae based on growth rate for the target chemical (EO 1-2.5). While the EO units have an impact on the toxicity of specific AEs, the score of this endpoint is based on the worst reported values for dodecyl alcohol, ethoxylated (EO < 3). GreenScreen® criteria classify chemicals as a High hazard for acute aquatic toxicity when acute aquatic toxicity values are greater than 1 to 10 mg/L (CPA 2018b). The confidence in the score is high as it is based on measured data on the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2023a
  - Dodecyl alcohol, ethoxylated (EO 1-2.5): 96-hour $LC_{50}$ (*Danio rerio*, zebrafish) = 2.427 mg/L (nominal) based on mortality (GLP-compliant, OECD Guideline 203) (Klimisch 1, reliable without restriction).
  - Dodecyl alcohol, ethoxylated (EO 1-2.5): 48-hour $LC_{50}$ (*Oryzias latipes*, Japanese rice fish) = 2.4 mg/L (nominal) based on mortality (GLP-unspecified, Japanese Industrial Standard (JIS) K0102 (1981) Testing methods for Industrial Wastewater) (Klimisch 2, reliable with restrictions).
  - Dodecyl alcohol, ethoxylated (EO 1-2.5): 48-hour $LC_{50}$ (*O. latipes*, Japanese rice fish) = 3.72 mg/L (nominal) based on mortality (GLP-unspecified) (Klimisch 2, reliable with restrictions).
  - Dodecyl alcohol, ethoxylated (EO 1-2.5): 48-hour $LC_{50}$ (*Poecilia reticulata,* guppy*)* = 8.61 mg/L (nominal) based on mortality (GLP-unspecified) (Klimisch 2, reliable with restrictions).
  - Dodecyl alcohol, ethoxylated (EO 1-2.5): 48-hour $EC_{50}$ (*Ceriodaphnia dubia*, water flea) = 9.131 mg/L (nominal) based on mobility (GLP-compliant, OECD Guideline 202) (Klimisch 1, reliable without restriction).
  - Dodecyl alcohol, ethoxylated (EO 1-2.5): 72-hour growth rate and biomass $EC_{50}$ (*Raphidocelis subcapitata*, green algae) = 2.737 and 1.225 mg/L, respectively, (nominal) (GLP-compliant, OECD Guideline 201) (Klimisch 1, reliable without restriction).
- HERA 2009
  - Acute toxicity data indicate that toxicity of AEs is expected to decrease with increasing EO number, provided the AEs remains soluble in water.
- Environment Canada 2013
  - The aquatic toxicity of AEs increases with decreasing ethoxylate chain length.
  - In general, aquatic plants tend to be less sensitive towards AEs than fish and aquatic invertebrates.
- CETOX 2001
  - Algae are the most sensitive trophic level for the aquatic toxicity of AEs, although the toxicity varies based on test conditions and species tested.

- The toxicity of AEs towards algae, aquatic invertebrates, and fish increases with decreasing EO chain length.

**Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L):** *H*
Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of High for chronic aquatic toxicity based on a growth rate NOEC of 0.5 mg/L in algae (EO 1-2.5). GreenScreen® criteria classify chemicals as a High hazard for chronic aquatic toxicity when chronic aquatic toxicity values are between 0.1 and 1 mg/L (CPA 2018b). The confidence in the score is low due to the lack of data for the fish and aquatic invertebrate trophic levels, and surfactants are out of the applicability domain of ECOSAR.
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 2023a
  - Dodecyl alcohol, ethoxylated (EO 1-2.5): 72-hour growth rate LOEC and NOEC (*Raphidocelis subcapitata*, green algae) = 1 and 0.5 mg/L, respectively (nominal) (GLP-compliant, OECD Guideline 201) (Klimisch 1, reliable without restriction).
- HERA 2009
  - *Aquatic Vertebrates*: Chronic aquatic toxicity values (survival and reproduction NOEC and EC10) for AEs (C9-15 and EO 6-9) toward aquatic vertebrates range from 0.079 to 8.983 mg/L.
  - *Aquatic Invertebrates*: Chronic aquatic toxicity values (reproduction, length gain, and survival NOEC or $EC_{10}$) for AEs (C9-15 and EO 6-10) towards aquatic invertebrates range from 0.062 to 3.635 mg/L.
  - *Green Algae/Aquatic Plants*: Chronic aquatic toxicity values (growth rate, cell density, or population size $EC_{10}$) for AEs (C8-15 and EO 3-9) towards green algae and aquatic plants range from 0.042 to 9.791 mg/L.
- Based on the weight of evidence, a score of High was assigned. Measured data are only identified for the algae trophic level for the target chemical (EO 1-2.5). However, as reported previously for acute aquatic toxicity, algae is the most sensitive trophic level. In addition, similar to acute aquatic toxicity, the EO chain length may also be negatively associated with the aquatic toxicity. Therefore, it is reasonable to conclude that dodecyl alcohol, ethoxylated (EO < 10) has chronic aquatic toxicity values in the range of High (0.1 – 1 mg/L) for all trophic levels. Similar AEs have a wide range of chronic aquatic toxicities, corresponding to scores of Moderate to Very High for all three trophic levels. Therefore, ToxServices relied solely on the measured data for the target chemical to score this endpoint.

## Environmental Fate (Fate)

**Persistence (P) Score (vH, H, M, L, or vL):** *vL*
Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Low for persistence based on ready biodegradability guideline studies (OECD Guideline 301C and 301D) in which the target chemical (EO 1-2.5) reached the pass level, but no data were identified for the 10-day window. However, the 10-day window does not apply to the OECD 301C test, and as a pragmatic approach, chemicals that pass this test are considered readily biodegradable (OECD 2001). GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when they mainly partition to water, soil or sediment, and are readily biodegradable within a 10-day window (CPA 2018b). The confidence in the score is low as it is based on dodecyl alcohol, ethoxylated with shorter EO chains (1-2.5), and longer EO chains may slow down the rate of degradation.

- 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 2023a
  - A ready biodegradability test conducted according to OECD Guideline 301 C / EU Method C.4-F (MITI test) (GLP unspecified) was performed with activated sludge (adaptation not specified) exposed to dodecyl alcohol, ethoxylated (1-2.5 EO) (purity unspecified) at 30 mg/L for 28 days. The level of degradation by BOD, TOC removal, and UV-Vis parameters were 74%, 44%, and 62% in 28 days. No information was provided for the 10-day window; however, the study authors concluded that the test substance was readily biodegradable under the conditions of this test (Klimisch 2, reliable with restrictions). *ToxServices notes the concept of the 10-day window does not apply to the MITI method, and, therefore, is not required to determine readily biodegradability status (OECD 2001).*
  - A ready biodegradability test conducted according to OECD Guideline 301 D (closed bottle test) (GLP unspecified) was performed with activated sludge (adaptation not specified) exposed to dodecyl alcohol, ethoxylated (1-2.5 EO) (purity unspecified) at > 2 - < 5 mg/L for 30 days. At the end of the exposure period, the level of degradation (BOD) was 74-84% in 30 days. No information was provided for the 10-day window; however, the study authors concluded that the test substance was readily biodegradable under the conditions of this test (Klimisch 2, reliable with restrictions).
- HERA 2009
  - AEs with typical alkyl chain length (C8-C18) and EO chain length 3-20 typically reach > 60% biodegradation in standard ready biodegradability tests, including OECD Guideline 301 tests. The percent biodegradation ranged from 60%-100%. HERA notes that the 10-day window is not applicable to commercial surfactants and thus does not report if this window is met.
- CETOX 2001
  - Linear AEs are easily degraded under aerobic conditions and degradation is relatively unaffected by the length of alkyl carbon chain and the number of EO units.
  - The length of the EO chain determines the water solubility of the AE, with longer EO chains decreasing the bioavailability of the AE. Reduced biodegradation is observed with > 20 EO units.

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

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Very Low for bioaccumulation based on the most conservative experimental BCF of 12.7 for a $C_{12}EO_8$ and a measured log $K_{ow}$ value of 2.26 for the target chemical (EO 1-2.5). GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when the BCF is less than 100 and log $K_{ow}$ is no greater than 4 (CPA 2018b). Confidence in the score is reduced because limited experimental details are available and due to the limitations in distinguishing between the parent compound and metabolites.

- 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 2023a
  - The authors of the ECHA dossier for dodecyl alcohol, ethoxylated (1-2.5 EO) reported a BCF of 81.7 L/kg; however, no information on the basis of this value was presented.

  - Dodecyl alcohol, ethoxylated (1-2.5 EO) has a log $K_{ow}$ value of 2.26 at 25°C and pH of 7.6 as identified in an OECD Guideline 117 (HPLC method) study (Klimisch 1, reliable without restriction).
- HERA 2009
  - BCF values in fathead minnows range from < 5 to 387.5 for $C_{12\text{-}16}EO_{4\text{-}14}$. For C12 AEs, the only value is 12.7 for $C_{12}EO_8$. HERA notes that bioconcentration studies may overestimate the bioconcentration factor due to the inability to distinguish between the parent compound and metabolites.
  - Log $K_{ow}$ values for surfactants are difficult to determine experimentally as they are located at the interfaces in an oil/water system. Therefore, predicted values are often used.
- Based on the weight of evidence, a score of Very Low was assigned. Although measurement and interpretation of the log $K_{ow}$ for a surfactant is challenging (HERA 2009), AEs are rapidly metabolized in aquatic organisms and therefore not expected to bioaccumulate. ToxServices used the measured BCF for of 12.7 for $C_{12}EO_8$ ethoxylated alcohol to evaluate this endpoint.

## Physical Hazards (Physical)

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

Dodecyl alcohol, ethoxylated (EO < 10) assigned a score of Low for reactivity based on ToxServices not classifying it as a reactive chemical under GHS criteria. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when no GHS classification is available (CPA 2018b). The confidence in the score is low due to lack of measured data for explosiveness.

- 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 2023a
  - The authors of the ECHA dossier reported that dodecyl alcohol, ethoxylated (1-2.5 EO) was non-explosive and non-oxidizing due to a lack of chemical groups associated with explosive and oxidizing properties, and non-oxidizing on the basis of its chemical structure. Additionally, no evidence of pyrophoric properties was identified by the authors of the ECHA dossier.
  - Dodecyl alcohol, ethoxylated (1-2.5 EO) did not catch fire at 27°C and a pressure of 966 hPa in an auto-ignition temperature (liquids) test (Klimisch 1, reliable without restriction).
- HSDB 2018
  - Dodecyl alcohol, ethoxylated has an instability rating of 0 from the National Fire Protection Association (NFPA) ("Normally stable, even under fire exposure conditions, and is not reactive with water").
- Based on the weight of evidence, ToxServices identified dodecyl alcohol, ethoxylated (EO < 10) as not reactive. Dodecyl alcohol, ethoxylated (1-2.5 EO) is not self-heating up to 27°C and pressure of 966 hPa. It is not expected to be explosive or self-reactive based on chemical structure and an NFPA instability rating of 0. Dodecyl alcohol, ethoxylated (1-2.5 EO) has no reactive functional groups that would make it oxidizing or explosive, and it is not a peroxide. As it is not explosive, it does not require desensitization. It is stable under recommended storage conditions. Overall, dodecyl alcohol, ethoxylated (1-2.5 EO) is GHS Not Classified for any of the reactivity sub endpoints(UN 2021). No data were found regarding corrosivity to metal.

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

Dodecyl alcohol, ethoxylated (EO < 10) was assigned a score of Low for flammability based on ToxServices not classifying it as a flammable chemical under GHS criteria. GreenScreen® criteria classify chemicals as a Low hazard for flammability when no GHS classification is available (CPA 2018b). The confidence in the score was high as it was based on measured data on the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2023a
  - Dodecyl alcohol, ethoxylated (1-2.5 EO) has a flash point of 112°C as determined in an ASTM D93 Pensky-Martens closed cup test. This study was reported by numerous peer-reviewed sources (Klimisch 1, reliable without restriction).
  - Dodecyl alcohol, ethoxylated (1-2.5 EO) has a boiling point of 242°C at 969.4 hPa in an OECD Guideline 103 test (Klimisch 1, reliable without restriction).
  - As previously described, dodecyl alcohol, ethoxylated (1-2.5 EO) did not catch fire at 27°C and a pressure of 966 hPa in an auto-ignition temperature (liquids) test (Klimisch 1, reliable without restriction).
- HSDB 2018
  - Dodecyl alcohol, ethoxylated has a measured flashpoint of >200°C (closed cup) and an NFPA fire rating of 1 ("Materials that must be preheated before ignition can occur. Materials require considerable preheating, under all ambient temperature conditions, before ignition and combustion can occur.").
- Based on the above data, including a flashpoint > 93°C, and a NFPA fire rating of 1, dodecyl alcohol, ethoxylated (1-2.5 EO) is not flammable or pyrophoric. Therefore, ToxServices did not classify dodecyl alcohol, ethoxylated (EO < 10) as a flammable liquid under GHS criteria (UN 2021).

**Use of New Approach Methodologies (NAMs)[8] in the Assessment, Including Uncertainty Analyses of Input and Output**

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

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

As shown in Table 4, Type I (input data) uncertainties in dodecyl alcohol, ethoxylated (EO < 10)'s NAMs dataset include limited experimental data for carcinogenicity, endocrine activity, and respiratory sensitization, and lack of established test methods for respiratory sensitization. Dodecyl alcohol, ethoxylated (EO < 10)'s Type II (extrapolation output) uncertainties include lack of defined applicability domains of OECD QSAR Toolbox and ToxCast models in examination of structural alerts, limitation of *in vitro* genotoxicity assays in mimicking *in vivo* metabolism and their focusing on one or only a few types of genotoxicity events, uncertain *in vivo* relevance of *in silico* receptor binding activity predictions, the limitations in the examination of structural alerts for respiratory sensitization evaluation that does not account for non-immunologic mechanisms of respiratory sensitization, and inability of individual *in vitro* skin irritation and eye irritation tests to completely differentiate certain GHS categories. Some of dodecyl alcohol, ethoxylated (EO < 10)'s type II uncertainties were alleviated by the use of *in vitro* test batteries and/or in combination of *in vivo* data.

| **Table 4: Summary of NAMs Used in the GreenScreen® Assessment, Including Uncertainty Analyses** | |
|---|---|
| **Uncertainty Analyses (OECD 2020)** | |
| **Type I Uncertainty: Data/Model Input** | **Carcinogenicity**: Only limited experimental data are available for the oral and dermal routes of exposure.<br>**Endocrine activity:** Insufficient *in vivo* data for hormone signaling pathways are available.<br>**Respiratory sensitization**: No experimental data are available and there are no validated test methods. |
| **Type II Uncertainty: Extrapolation Output** | **Carcinogenicity**: OECD Toolbox structural alerts screening does not define applicability domains.<br>**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 |

[8] 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).

| | | |
|---|---|---|
| | does not entirely mimic *in vivo* conditions[9]. 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).[10] The *in vitro* chromosome aberration assay (OECD Guideline 473) does not measure aneuploidy and it only measures structural chromosomal aberrations. The exogenous metabolic activation system does not entirely mirror *in vivo* metabolism[11].<br>**Endocrine activity:** ToxCast models don't define applicability domain. The *in vivo* relevance of *in silico* receptor binding activity is uncertain due to lack of toxicokinetic considerations.<br>**Skin irritation**: The OECD Guideline 439 test is only used to identify irritating substances (GHS Category 2) and non-irritating substances (no category), and does not allow the classification as a mild skin irritant (GHS Category 3)[12].<br>**Eye irritation**: The BCOP (OECD Guideline 437) test is not recommended for identifying GHS Category 2A or 2B irritants[13]. The RhCE test (OECD Guideline 492) cannot differentiate between Category 2 and Category 1, or between Category 2A and Category 2B. There is no single *in vitro* method that can replace an *in vivo* eye irritation test[14]. Therefore, this method is not recommended for identifying eye irritants (Category 2) or substances causing serious eye damage (Category 1) (ECHA 2017).<br>**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 | Y | *In silico* modeling: OECD Toolbox |
| Mutagenicity | Y | *In vitro* data: Bacterial reverse mutation assay/*in vitro* gene mutation assay/*in vitro* chromosome aberration assay |
| Reproductive toxicity | N | |

[9] https://www.oecd-ilibrary.org/docserver/9789264071247-en.pdf?expires=1614097593&id=id&accname=guest&checksum=89925F80B9F4BD2FFC6E90F94A0EE427
[10] https://www.oecd-ilibrary.org/docserver/9789264264809-en.pdf?expires=1614097800&id=id&accname=guest&checksum=C0DE371FB9C5A878E66C9AB7F84E6BBE
[11] https://www.oecd-ilibrary.org/docserver/9789264264649-en.pdf?expires=1614098015&id=id&accname=guest&checksum=6A4F9CE52EA974F5A74793DD54D54352
[12] https://www.oecd-ilibrary.org/docserver/9789264242845-en.pdf?expires=1614097324&id=id&accname=guest&checksum=D664A7EDCDE297919BE9A478941EBEC6
[13] https://www.oecd-ilibrary.org/docserver/9789264203846-en.pdf?expires=1614095760&id=id&accname=guest&checksum=1613168F64BDB3558225572BDD75FC8D
[14] https://www.oecd.org/env/ehs/testing/E492_2017.pdf

| | | |
|---|---|---|
| Developmental toxicity | N | |
| Endocrine activity | Y | *In silico* modeling: ToxCast models/ Danish QSAR |
| 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/Danish QSAR |
| Skin irritation | Y | *In vitro* testing: OECD Guideline 439 RhE test |
| Eye irritation | Y | *In vitro* testing: OECD Test Guideline 492 reconstructed human cornea-like epithelium test (EpiOcular™) / bovine corneal opacity and permeability (BCOP) test |
| Acute aquatic toxicity | N | |
| Chronic aquatic toxicity | N | |
| Persistence | Y | Non-animal testing: OECD 301C, D Biodegradation tests |
| Bioaccumulation | N | |

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## APPENDIX A: Hazard Classification Acronyms
**(in alphabetical order)**

**(AA) Acute Aquatic Toxicity**

**(AT) Acute Mammalian Toxicity**

**(B) Bioaccumulation**

**(C) Carcinogenicity**

**(CA) Chronic Aquatic Toxicity**

**(D) Developmental Toxicity**

**(E) Endocrine Activity**

**(F) Flammability**

**(IrE) Eye Irritation/Corrosivity**

**(IrS) Skin Irritation/Corrosivity**

**(M) Mutagenicity and Genotoxicity**

**(N) Neurotoxicity**

**(P) Persistence**

**(R) Reproductive Toxicity**

**(Rx) Reactivity**

**(SnS) Sensitization- Skin**

**(SnR) Sensitization- Respiratory**

**(ST) Systemic/Organ Toxicity**

# APPENDIX B: Results of Automated GreenScreen® Score Calculation for Dodecyl Alcohol, Ethoxylated (EO < 10) (CAS #9002-92-0)

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 | Dodecyl alcohol, ethoxylated (EO <10) | 9002-92-0 | L | L | L | *M* | DG | M | *M* | L | *L* | *M* | L | *L* | L | *H* | H | *H* | *vL* | *vL* | *L* | L |

**Table 3: Hazard Summary Table**

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

**Table 4**

| Chemical Name | Preliminary GreenScreen® Benchmark Score |
|---|---|
| Dodecyl alcohol, ethoxylated (EO <10) | 2 |

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

**Table 6**

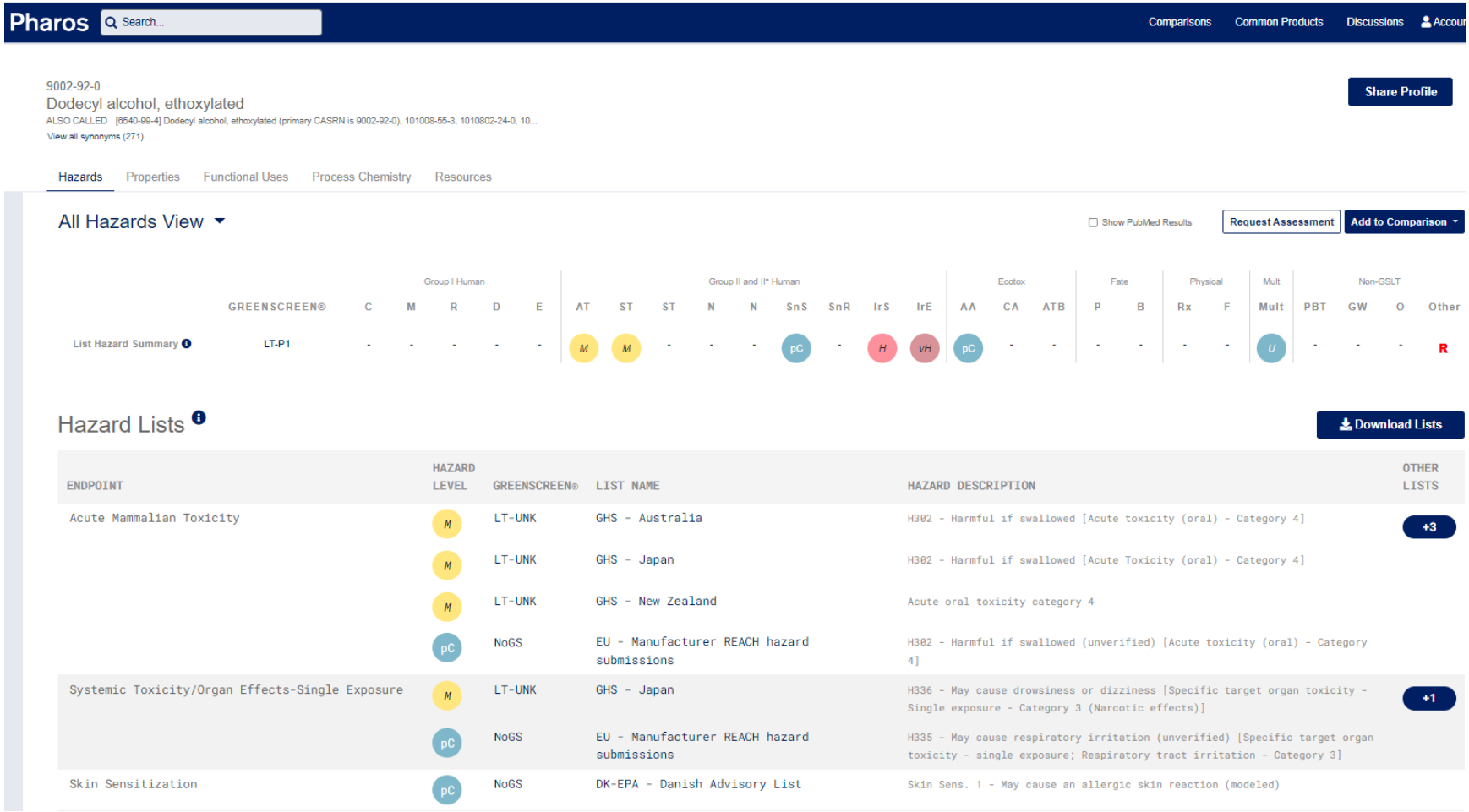
| Chemical Name | Final GreenScreen® Benchmark Score |
|---|---|
| Dodecyl alcohol, ethoxylated (EO <10) | 2 |

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 Dodecyl Alcohol, Ethoxylated (EO < 10) (CAS #9002-92-0)



Pharos | Search... | Comparisons | Common Products | Discussions | Accou

9002-92-0
Dodecyl alcohol, ethoxylated
ALSO CALLED [6540-99-4] Dodecyl alcohol, ethoxylated (primary CASRN is 9002-92-0), 101008-55-3, 1010802-24-0, 10...
View all synonyms (271)

Share Profile

Hazards | Properties | Functional Uses | Process Chemistry | 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 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | GREENSCREEN® | 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 |
| List Hazard Summary | LT-P1 | - | - | - | - | - | M | M | - | - | - | pC | - | H | vH | pC | - | - | - | - | - | - | U | - | - | - | R |

## Hazard Lists

Download Lists

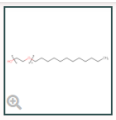
| ENDPOINT | HAZARD LEVEL | GREENSCREEN® | LIST NAME | HAZARD DESCRIPTION | OTHER LISTS |
|---|---|---|---|---|---|
| Acute Mammalian Toxicity | M | LT-UNK | GHS - Australia | H302 - Harmful if swallowed [Acute toxicity (oral) - Category 4] | +3 |
| | M | LT-UNK | GHS - Japan | H302 - Harmful if swallowed [Acute Toxicity (oral) - Category 4] | |
| | M | LT-UNK | GHS - New Zealand | Acute oral toxicity category 4 | |
| | pC | NoGS | EU - Manufacturer REACH hazard submissions | H302 - Harmful if swallowed (unverified) [Acute toxicity (oral) - Category 4] | |
| Systemic Toxicity/Organ Effects-Single Exposure | M | LT-UNK | GHS - Japan | H336 - May cause drowsiness or dizziness [Specific target organ toxicity - Single exposure - Category 3 (Narcotic effects)] | +1 |
| | pC | NoGS | EU - Manufacturer REACH hazard submissions | H335 - May cause respiratory irritation (unverified) [Specific target organ toxicity - single exposure; Respiratory tract irritation - Category 3] | |
| Skin Sensitization | pC | NoGS | DK-EPA - Danish Advisory List | Skin Sens. 1 - May cause an allergic skin reaction (modeled) | |

| | | | | | |
|---|---|---|---|---|---|
| Skin Irritation/Corrosivity | H | LT-UNK | GHS - Australia | H315 - Causes skin irritation [Skin corrosion/irritation - Category 2] | +1 |
| | pC | NoGS | EU - Manufacturer REACH hazard submissions | H315 - Causes skin irritation (unverified) [Skin corrosion/irritation - Category 2] | |
| Eye Irritation/Corrosivity | vH | LT-UNK | GHS - Australia | H318 - Causes serious eye damage [Serious eye damage/eye irritation - Category 1] | +3 |
| | vH | LT-UNK | GHS - New Zealand | Serious eye damage category 1 | |
| | pC | NoGS | EU - Manufacturer REACH hazard submissions | H318 - Causes serious eye damage (unverified) [Serious eye damage/eye irritation - Category 1] | |
| | pC | NoGS | EU - Manufacturer REACH hazard submissions | H319 - Causes serious eye irritation (unverified) [Serious eye damage/eye irritation - Category 2A] | |
| Acute Aquatic Toxicity | pC | NoGS | DK-EPA - Danish Advisory List | Aquatic Acute1 - Very toxic to aquatic life (modeled) | +2 |
| | pC | NoGS | DK-EPA - Danish Advisory List | Aquatic Chronic1 - Very toxic to aquatic life with long lasting effects (modeled) | |
| | pC | NoGS | EU - Manufacturer REACH hazard submissions | H400 - Very toxic to aquatic life (unverified) [Hazardous to the aquatic environment (acute) - Category 1] | |
| Carcinogenicity,Mutagenicity/Genotoxicity Reproductive Toxicity, Developmental Toxicity, Acute Mammalian Toxicity, or System Toxicity/Organ Effects. | U | LT-UNK | EC - CEPA DSL | Inherently Toxic to Humans (iTH) | |
| Acute aquatic toxicity; Chronic aquatic toxicity | U | LT-UNK | EC - CEPA DSL | Inherently Toxic in the Environment (iTE) | |
| 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 | H410 - Very toxic to aquatic life with long lasting effects (unverified) [Hazardous to the aquatic environment (chronic) - Category 1] | +2 |
| | pC | NoGS | EU - Manufacturer REACH hazard submissions | H411 - Toxic to aquatic life with long lasting effects (unverified) [Hazardous to the aquatic environment (chronic) - Category 2] | |
| | pC | NoGS | EU - Manufacturer REACH hazard submissions | H412 - Harmful to aquatic life with long lasting effects (unverified) [Hazardous to the aquatic environment (chronic) - Category 3] | |
| 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 | |

## APPENDIX D: OECD Toolbox Profiling Results for Dodecyl Alcohol, Ethoxylated (EO < 10) (CAS #9002-92-0)

| Filter endpoint tree... | 1 [target] |
|---|---|
| Structure |  |
| **Structure info** | |
| **Additional Ids** | |
| **CAS Number** | 9002-92-0 |
| **CAS-SMILES relation** | High |
| **Chemical name(s)** | 9002-92-0 |
| **Identity** | Sources:13 |
| **Molecular formula** | C14H30O2 |
| **Predefined substance type** | Mono constituent |
| **SMILES** | CCCCCCCCCCCCOCCO |
| **Parameters** | |
| **Physical Chemical Properties** | |
| **Environmental Fate and Transport** | |
| **Ecotoxicological Information** | |
| **Human Health Hazards** | |
| **Profiling** | |
| **Predefined** | |
| **Database Affiliation** | Aquatic ECETOC |
| **Inventory Affiliation** | AIIC |
| **OECD HPV Chemical Categories** | Monoethylene glycol ethers |
| **Substance type** | Discrete chemical |
| **US-EPA New Chemical Categories** | Nonionic Surfactants |
| **Endpoint Specific** | |
| **Carcinogenicity (genotox and nongenotox) alerts by ISS** | No alert found |
| **Oncologic Primary Classification** | Not classified |
| **Respiratory sensitisation** | No alert found |
| **Metabolism/Transformation** | |
| **Hydrolysis simulator (acidic)** | 0 metabolite(s) |
| **Hydrolysis simulator (basic)** | 0 metabolite(s) |
| **Hydrolysis simulator (neutral)** | 0 metabolite(s) |

## APPENDIX E: ToxCast Model Results for Dodecyl Alcohol, Ethoxylated (EO < 10) (CAS #9002-92-0)



**Polyoxyethylene dodecyl mono ether**

9002-92-0 | DTXSID2025218

Searched by CASRN

**Bioactivity - ToxCast: Models**

EXPORT

**ToxCast Model Predictions**

| Model | Receptor | Agonist | Antagonist | Binding |
|---|---|---|---|---|
| CERAPP Potency Level (From Literature) | Estrogen | Inactive | Inactive | Inactive |
| CERAPP Potency Level (Consensus) | Estrogen | 0.00 | 0.00 | 0 |

## APPENDIX F: Danish QSAR Endocrine Results for Dodecyl Alcohol, Ethoxylated (EO < 10) (CAS #9002-92-0)

| | Exp | Battery | CASE Ultra | Leadscope | SciQSAR |
|---|---|---|---|---|---|
| Estrogen Receptor α Binding, Full training set (Human *in vitro*) | | NEG_OUT | NEG_IN | NEG_OUT | INC_OUT |
| Estrogen Receptor α Binding, Balanced Training Set (Human *in vitro*) | | NEG_IN | NEG_IN | NEG_OUT | NEG_IN |
| Estrogen Receptor α Activation (Human *in vitro*) | | INC_OUT | NEG_IN | NEG_OUT | POS_IN |
| Estrogen Receptor Activation, CERAPP data (*in vitro*) | | N/A | N/A | NEG_IN | N/A |
| Androgen Receptor Inhibition (Human *in vitro*) | | NEG_IN | NEG_IN | NEG_IN | 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 |
| Sodium/iodide symporter (NIS), higher sensitivity | | N/A | N/A | INC_OUT | N/A |
| Sodium/iodide symporter (NIS), higher specificity | | N/A | N/A | INC_OUT | N/A |
| Thyroid Receptor α Binding (Human *in vitro*) | | | | | |
| - mg/L | | | 36852.22 | 2537.195 | 11702.1 |
| - µM | | | 159955.8 | 11012.61 | 50792.55 |
| - Positive for $IC_{50}$ ≤ 10 µM | | | | | |
| - Positive for $IC_{50}$ ≤ 100 µM | | | | | |
| - Domain | | OUT | OUT | OUT | OUT |
| Thyroid Receptor β Binding (Human *in vitro*) | | | | | |
| - mg/L | | 3846.116 | 7455.278 | 104.1271 | 236.9538 |
| - µM | | 16693.94 | 32359.38 | 451.9601 | 1028.49 |
| - Positive for $IC_{50}$ ≤ 10 µM | | | | | |
| - Positive for $IC_{50}$ ≤ 100 µM | | | | | |
| - Domain | | IN | IN | OUT | IN |
| 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 | NEG_IN | N/A |
| Pregnane X Receptor (PXR) Binding (Human *in vitro*) | N/A | NEG_IN | NEG_IN | NEG_OUT | NEG_IN |

| | Exp | Battery | CASE Ultra | Leadscope | SciQSAR |
|---|---|---|---|---|---|
| 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 |
| Pregnane X Receptor (PXR) Activation (Rat *in vitro*) | | N/A | N/A | NEG_IN | N/A |
| CYP3A4 Induction (Human *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 |

## APPENDIX G: Danish QSAR Sensitization Results for Dodecyl Alcohol, Ethoxylated (EO < 10) (CAS #9002-92-0)

| | |
|---|---|
| Protein binding by OASIS, alerts in: | |
| - parent only | No alert found |
| - metabolites from skin metabolism simulator only | Aldehydes |
| - metabolites from auto-oxidation simulator only | Aldehydes; Hydroperoxides |
| Protein binding by OECD, alerts in: | |
| - parent only | No alert found |
| - metabolites from skin metabolism simulator only | Mono-carbonyls |
| - metabolites from auto-oxidation simulator only | Mono-carbonyls |
| Protein binding potency Cys (DRPA 13%), alerts in: | |
| - parent only | DPRA less than 9% (DPRA 13%) >> Alcohols |
| - metabolites from skin metabolism simulator only | DPRA above 21% (DPRA 13%) >> Non-Conjugated monoaldehydes (reactive); DPRA less than 9% (DPRA 13%) >> Non-Conjugated carboxylic acids and esters (non reactive) |
| - metabolites from auto-oxidation simulator only | DPRA above 21% (DPRA 13%) >> Non-Conjugated monoaldehydes (reactive); DPRA less than 9% (DPRA 13%) >> Alcohols; DPRA less than 9% (DPRA 13%) >> Non-Conjugated monoaldehydes (non reactive) |
| Protein binding potency Lys (DRPA 13%), alerts in: | |
| - parent only | DPRA less than 9% (DPRA 13%) >> Alcohols; DPRA less than 9% (DPRA 13%) >> Nonionic surfactants |
| - metabolites from skin metabolism simulator only | DPRA less than 9% (DPRA 13%) >> Non-alpha,beta-conjugated monoaldehydes (non reactive); DPRA less than 9% (DPRA 13%) >> Non-Conjugated carboxylic acids and esters (non reactive) |
| - metabolites from auto-oxidation simulator only | DPRA less than 9% (DPRA 13%) >> Alcohols; DPRA less than 9% (DPRA 13%) >> Non-alpha,beta-conjugated monoaldehydes (non reactive); DPRA less than 9% (DPRA 13%) >> Nonionic surfactants; Grey zone 9-21% (DPRA 13%) >> Non-alpha,beta-conjugated monoaldehydes (Grey zone) |
| Keratinocyte gene expression, alerts in: | |
| - parent only | Not possible to classify according to these rules |
| - metabolites from skin metabolism simulator only | High gene expression >> Non-conjugated aldehydes and dialdehydes; Moderate gene expression >> Fragrance aldehydes |
| - metabolites from auto-oxidation simulator only | High gene expression >> Non-conjugated aldehydes and dialdehydes; Moderate gene expression >> Fragrance aldehydes |
| Protein binding potency GSH, alerts in: | |
| - parent only | Not possible to classify according to these rules (GSH) |

*OECD QSAR Toolbox v.4.1 profilers*

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

## Irritation and Sensitization

| | Exp | Battery | CASE Ultra | Leadscope | SciQSAR |
|---|---|---|---|---|---|
| Severe Skin Irritation in Rabbit | NEG | NEG_IN | NEG_IN | NEG_IN | NEG_IN |
| Skin sensitisation GHS/CLP at least Cat. 1, LLNA-based (open data only) | | | | POS_IN | |
| Skin sensitisation GHS/CLP at least Cat. 1, LLNA-based (open data and REACH-registrations) | N/A | | | INC_OUT | |
| Skin sensitisation GHS/CLP at least Cat. 1, LLNA-based, only negative predictions (open data only) | | | | N/A | |
| Skin sensitisation GHS/CLP Cat. 1A, LLNA-based (open data only) | | | | NEG_IN | |
| Skin sensitisation GHS/CLP Cat. 1A, LLNA-based (open data and REACH-registrations) | N/A | | | NEG_IN | |
| Skin sensitisation GHS/CLP Cat. 1A, LLNA-based, only positive predictions (open data and REACH-registrations) | N/A | | | N/A | |
| Allergic Contact Dermatitis in Guinea Pig and Human* | N/A | NEG_IN | NEG_IN | NEG_IN | NEG_IN |
| Respiratory Sensitisation in Humans | | NEG_IN | NEG_OUT | NEG_IN | NEG_IN |

*DTU-developed models*

**Based on commercial training set*

## APPENDIX H: Change in Benchmark Score

Table 5 provides a summary of changes to ToxServices' GreenScreen® Benchmark™ for dodecyl alcohol, ethoxylated (EO < 10). This is a new GreenScreen® assessment.

**Table 5: Change in GreenScreen® Benchmark™ for Dodecyl Alcohol, Ethoxylated (EO < 10)**

| Date | GreenScreen® Benchmark™ | GreenScreen® Version | Comment |
|---|---|---|---|
| August 28, 2023 | BM-2 | v. 1.4 | Original assessment |

**Licensed GreenScreen® Profilers**

**Dodecyl Alcohol, Ethoxylated (EO < 10) GreenScreen® Evaluation Prepared by:**

SIGNATURE BLOCK

Deb Remeikas, M.A.
Toxicologist
ToxServices LLC

**Dodecyl Alcohol, Ethoxylated (EO < 10) GreenScreen® Evaluation QC'd by:**

SIGNATURE BLOCK

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