LINEAR (C12 AND C14) ALKYL ALCOHOLS, ETHOXYLATED (6EO)

(CAS #68439-50-9)

GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

ToxServices LLC

Assessment Date: April 21, 2021

Expiration Date: April 21, 2026

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TABLE OF CONTENTS

TABLE OF FIGURES

TABLE OF TABLES

GreenScreen® Executive Summary for Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO) (CAS #68439-50-9)

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) is a nonionic surfactant that is used as an emulsifier, solubilizing agent, and cleaning agent. It also functions as a solvent, coupling agent, or chemical intermediate. It is a clear liquid that is non-flammable, non-reactive, and non-volatile.

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) 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 Health Hazard (developmental toxicity-D)

Data gaps (DG) exist for endocrine activity-E and neurotoxicity (repeated dose)-Nr*. As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gaps. In a worst-case scenario, if linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

The New Approach Methodology (NAM) used in this GreenScreen® includes *in silico* modeling for respiratory sensitization. The quality, utility, and accuracy of NAM predictions are greatly influenced by two primary types of uncertainties:

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

Type I (input data) uncertainties in linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO)'s NAMs dataset include the absence of experimental data for respiratory sensitization. Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO)'s Type II (extrapolation output) uncertainties are that OECD Toolbox only identifies structural alerts, and does not define applicability domains.

GreenScreen® Hazard Summary Table for Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO)

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

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

GreenScreen® Chemical Assessment for Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO) (CAS #68439-50-9)

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

GreenScreen® Assessment (v.1.4) Prepared By:
Name: Sara M. Ciotti, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: March 15, 2021

Quality Control Performed By:
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Title: Senior Toxicologist
Organization: ToxServices LLC
Date: March 17, 2021

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Name: Bingxuan Wang, Ph.D., D.A.B.T.
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Date: April 15, 2021

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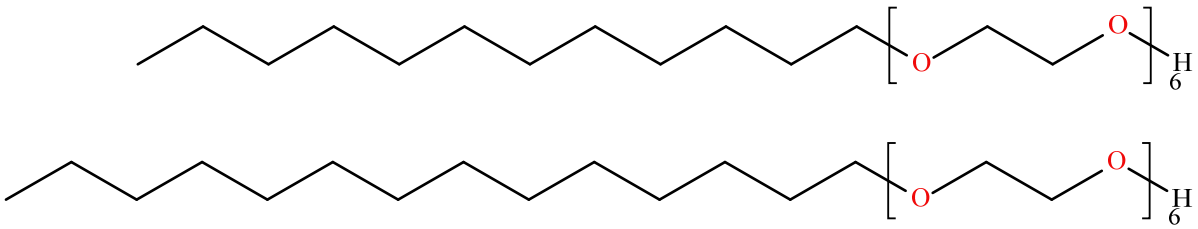
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: April 21, 2021

Expiration Date: April 21, 2026[2]

Chemical Name: Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO)

CAS Number: 68439-50-9

Chemical Structure(s):



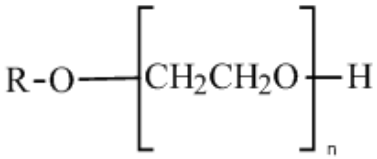
Also called: Ethoxylated C12-14 alcohols, Linear (C12 and C14) alkyl alcohols, ethoxylated; alcohols, C12-14, ethoxylated; alpha-alkyl-omega-hydroxypoly(oxypropylene) and/or poly(oxyethylene) (ChemIDplus 2021)

Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):
Limited data were available regarding the toxicity of linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO). Therefore, linear alkyl alcohol alkoxylates (AAAs) with a similar number of carbons and ethylene oxide (EO) units (polyethoxylate, POE) were used as surrogates.

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

The human health hazards of AAAs as a group have been assessed by the United States Environmental Protection Agency (U.S. EPA) and Human and Enviromental Risk Assessment (HERA) (U.S. EPA 2009, HERA 2009). Sufficient data were availble for similar AAAs to assign a Benchmark Score.

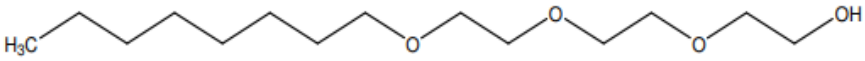
No specific chemical structures are available for the surrogates used in this assessment as commercial nonionic surfactants are normally a mixture of homologous structures with unknown or variable composition. Representative chemical structures for alcohol ethoxylates (AAAs POE) and alcohol ethoxylates evaluated by HERA (2009) are shown below.



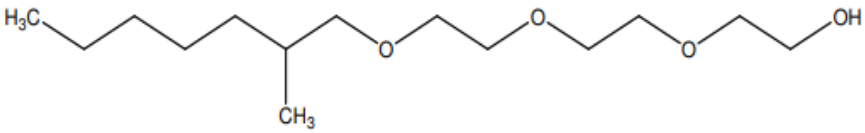
Representative structure for AAAs POE (U.S. EPA 2009)

where:

R = linear, essentially linear or branched alkyl chain
n = average number of ethylene oxide units



Linear AE (C_8EO_3)



Essential linear, methyl branched AE (C_8EO_3)

Identify Applications/Functional Uses:

1. Surfactant
2. Solvent
3. Coupling agent
4. Chemical intermediate

Known Impurities[3]:

Polyethylene oxides may contain residual ethylene oxide and/or 1,4-dioxane. The screen is performed on the theoretical pure substance.

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

GreenScreen® Summary Rating for Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO)[4,5,6,7]: Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) 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 Health Hazard (developmental toxicity-D)

Data gaps (DG) exist for endocrine activity-E and neurotoxicity (repeated dose)-Nr*. As outlined in GreenScreen® Guidance (CPA 2018b) Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gaps. In a worst-case scenario, if linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Summary Table for Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO)

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

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

Environmental Transformation Products

Alcohol ethoxylates are not expected to undergo abiotic degradation such as hydrolysis and photolysis in water, soil, sediment, or air (HERA 2009). They are rapidly biodegradable and therefore not likely to form relevant environmental transformation products.

Introduction

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) is a mixture of ethoxylated linear alcohols with a carbon chain length of 12 and 14. It is a nonionic surfactant used as an emulsifier, solubilizing agent, and cleansing agent. It can also function as a solvent, coupling agent or chemical intermediate (CIR 2012). Alkyl PEG ethers are mainly produced through alkaline catalysis by addition of ethylene oxide to a dry solution of the appropriate alcohol (i.e., C12 and C14 alcohols for this particular ingredient) with an alkali earth metal such as potassium hydroxide or an alkoxide such as sodium methoxide until the ethylene oxide is consumed or the reaction is terminated by addition of an acid (CIR 2012). This

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

assessment is for linear (C12 and C14) alkyl alcohols, ethoxylated ingredients that contain an average of 6 moles ethylene oxide.

ToxServices assessed linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) against GreenScreen® Version 1.4 (CPA 2018b) following procedures outlined in ToxServices' SOPs (GreenScreen® Hazard Assessment) (ToxServices 2020).

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

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

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) is listed on the SCIL with a full green circle as a surfactant.

GreenScreen® List Translator Screening Results

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen Benchmark™ 1 chemicals (CPA 2018b). Pharos (Pharos 2021) is an online list-searching tool that is used to screen chemicals against all of the lists in the List Translator electronically. ToxServices also checks the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b),[8] which are not considered GreenScreen® Specified Lists but are additional information sources, in conjunction with the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) can be found in Appendix C.

- Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) is an LT-P1 chemical when screened using Pharos, and therefore a full GreenScreen® is required.
- Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) is not listed on the U.S. DOT list.
- Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) 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
    - GHS – New Zealand: 9.1A (algal) – Very ecotoxic in the aquatic environment
    - GHS – New Zealand – 9.1A (other) – Very ecotoxic in the aquatic environment
    - GHS – New Zealand – 9.1D (crustacean) – Slightly harmful in the aquatic environment or are otherwise designated for biocidal action
    - GHS – New Zealand – 9.1D (fish) – Slightly harmful in the aquatic environment or are otherwise designated for biocidal action

Hazard Statement and Occupational Control

No harmonized Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statements were identified for linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO); however, the largest aggregate of notifications provided by companies to European Chemicals Agency (ECHA) in

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

REACH registrations, classified it as an eye irritant and acute aquatic toxicant as indicated in Table 1. General personal protective equipment (PPE) recommendations are presented in Table 2, below. No occupational exposure limits (OEL) were identified.

Table 1: GHS H Statements for Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO) (CAS #68439-50-9) (ECHA 2021a)

H Statement	H Statement Details
H319	Causes serious eye irritation
H400	Very toxic to aquatic life

Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO) (CAS #68439-50-9)

Personal Protective Equipment (PPE)	Reference	Occupational Exposure Limits (OEL)	Reference
Appropriate gloves; tightly fitting safety goggles; protective clothing	ECHA 2021a	None identified	

Physicochemical Properties of Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO)

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) is expected to be a clear liquid that is soluble in water. In general, alcohol ethoxylates typically have low vapor pressures, indicating a low potential to form vapors (HERA 2009). The water solubility and partition coefficient of alcohol ethoxylates varies by the number of EO units and carbon chain lengths, with longer carbon chain length homologues being less water soluble and EO chains increasing the water solubility (HERA 2009).

Table 3: Physical and Chemical Properties of Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO) (CAS #68439-50-9)

Property	Value	Reference
Molecular formula	Multiple	
SMILES Notation	Multiple	
Molecular weight	Varies	
Physical state	Liquid [a]	ECHA 2021b
Appearance	Clear liquid [a]	ECHA 2021b
Melting point	-6.18 – 10.75°C (measured)[a]	ECHA 2021b
Boiling point	266.95 – 400°C (measured)[a]	ECHA 2021b
Vapor pressure	0.011 mm Hg (measured)[a]	ECHA 2021b
Water solubility	7 – 63 mg/L (measured)[a]	ECHA 2021b
Dissociation constant	N/A	
Density/specific gravity	0.87 – 0.90 at 20°C (measured)[a]	ECHA 2021b
Partition coefficient	4.73-5.81 (estimates)	HERA 2009
Supplier, Tradename(s)	N/A	
Ethoxylated or propoxylated?	Ethoxylated	
# EO Units	6	
# PO Units	0	
EO/PO Ratio	N/A	
[a] Data are for the surrogate $C_{12\text{-}14}EO_{1\text{-}2.5}$		

Toxicokinetics

No information was found on the toxicokinetics of linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO), specifically. However, studies of analog compounds C12 alkyl ethoxylates (3-10EO), C14-18 (10EO), and C12-15 (6-7EO), alcohol ethoxylates demonstrated rapid and extensive absorption (>75%) in the gastrointestinal tract following oral administration, and rapid excretion via the urine and feces. Longer alkyl chain lengths, as well as greater degrees of ethoxylation, resulted in a higher proportion being excreted in expired air and less in urine. Absorption was decreased in quantity and speed following dermal application, but distribution and excretion followed a similar pattern (HERA 2009).

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

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

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Low for carcinogenicity based on a lack of carcinogenicity in long term studies with alcohol ethoxylate surrogates supported by a lack of structural alerts. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as the data are consistent and it is based on expert judgement by HERA and the U.S. EPA.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- U.S. EPA 2009
  - AAAs are not carcinogenic based on lack of structural alerts to carcinogenicity and reliable negative mutagenicity studies.
- HERA 2009
  - *Oral*
    - *Surrogate:* $C_{14\text{-}15}EO_7$: In a 1- and 2-year dietary study in Charles River rats (65/sex/dose), animals received $C_{14\text{-}15}EO_7$ in the diet at 0, 0.1, 0.5 or 1%. No increase in tumor incidence or other treatment-related pathologies were observed.
    - *Surrogate:* $C_{14\text{-}15}EO_7$: In a 2-year dietary study in Sprague-Dawley rats (100/sex/dose), animals received $C_{14\text{-}15}EO_7$ in the diet at 0, 0.1, 0.5 or 1%. No evidence of carcinogenic activity was observed. No further details were reported.
    - *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.
  - Alcohol ethoxylates are not carcinogenic based on lack of structural alerts to carcinogenicity, long term carcinogenicity studies, and reliable negative mutagenicity studies.

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

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Low for mutagenicity/genotoxicity based on negative results in bacterial reverse mutation assays, *in vitro* mammalian cell mutagenicity assay, *in vitro* chromosome aberration assays, and *in vivo* chromosome aberration assays for alcohol ethoxylates. 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). Confidence in the score is high as the data are consistent and the score 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
  - A large number of *in vivo* and *in vitro* mutagenicity and chromosomal aberration studies were conducted on alcohol ethoxylates (AEs). None of them showed a potential for genotoxicity. These assays in 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 alcohol ethoxylates.

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

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Low for reproductive toxicity based on the absence of adverse reproductive effects in reproductive toxicity studies performed with alcohol ethoxylates. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on reliable data.

- 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
  - *Surrogate: $C_{14\text{-}15}EO_7$*: In a two-generation study, Charles River CD rats (25/sex/dose for treated rats and 6/sex/dose for controls) were given $C_{14\text{-}15}EO_7$ in the diet at 0, 0.05%, 0.1% or 0.5% (equivalent to 0, 25, 50 or 250 mg/kg/day, according to HERA). 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. Females continuously exposed to the highest dose had slightly reduced body weight gain, and their pups had significantly lower 21-day body weight gain. F1 generation at the highest continuous feeding dose had increased relative liver weights in both sexes at the 91-day sacrifice, and F2 generations of the same group had increased relative liver weight at the 60-day caesarean section sacrifices. No histological changes were found in F0 and F1 animals.

It was concluded that there was no evidence of reproductive toxicity in the study, and HERA established the NOAEL at 0.5% (250 mg/kg/day).

- *Surrogate: $C_{12}EO_6$:* In a similarly designed study as above, $C_{12}EO_6$ was given to rats (number and strain not specified) by gavage 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, the NOAEL for reproductive toxicity was established at 250 mg/kg/day by HERA.
- *Surrogate: $C_{9\text{-}11}EO_6$:* In a GLP-compliant 2-generation study, weanling Fisher 344 rats (30/sex/dose) were dermally exposed to $C_{9\text{-}11}EO_6$ at 0, 1, 10 or 25% w/v (equivalent to 0, 10, 100 or 250 mg/kg/day, according to HERA) three times per week except during the mating periods. There were no compound-related reproductive effects on mating and fertility indices, mean gestational length in both generations, testicular weights, sperm counts, LDH-X activities, and macroscopic and microscopic examinations of reproductive organs. There were no compound-related developmental effects on litter size, number of live pups and sex ratio in F1 and F2 generations. Therefore, HERA established the NOAEL at 250 mg/kg/day for both reproductive and developmental toxicities.
- *Surrogate: $C_{12}EO_6$*: 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.
- *Surrogate: AAAs (CAS #Multiple):* 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*
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Moderate for developmental toxicity based on decreased pup weight following maternal exposure to alcohol ethoxylate surrogates in rats. 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). The confidence in the score is 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.
- HERA 2009
  - *Surrogate: $C_{14\text{-}15}EO_7$*: In a two-generation study, Charles River CD rats (25/sex/dose for treated rats and 6/sex/dose for controls) were given $C_{14\text{-}15}EO_7$ in the diet at 0, 0.05%, 0.1% or 0.5% (equivalent to 0, 25, 50 or 250 mg/kg/day, according to HERA). 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. Females continuously exposed to the highest dose had slightly reduced body weight gain, and their pups had significantly lower 21-day body weight gain. F1 generation at the highest continuous feeding dose had increased relative liver weights in both sexes at the 91-day sacrifice, and F2 generations of the same group had increased relative liver weight at the 60-day caesarean section sacrifices. No histological changes were found in F0 and F1 animals. Based on changes in body weight gain and relative liver weight, HERA established the NOAEL and LOAEL of 50 and 250 mg/kg/day, respectively, for developmental and maternal toxicity.

- *Surrogate: $C_{12}EO_6$*: In a similarly designed study as above, $C_{12}EO_6$ was given to rats (number and strain not specified) by gavage 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.
- *Surrogate: $C_{9\text{-}11}EO_6$*: In a GLP-compliant 2-generation study, weanling Fisher 344 rats (30/sex/dose) were dermally exposed to $C_{9\text{-}11}EO_6$ at 0, 1, 10 or 25% w/v (equivalent to 0, 10, 100 or 250 mg/kg/day, according to HERA) three times per week except during the mating periods. There were no compound-related reproductive effects on mating and fertility indices, mean gestational length in both generations, testicular weights, sperm counts, LDH-X activities, and macroscopic and microscopic examinations of reproductive organs. There were no compound-related developmental effects on litter size, number of live pups and sex ratio in F1 and F2 generations. Therefore, HERA established the NOAEL at 250 mg/kg/day for both reproductive and developmental toxicities.
- *Surrogate: $C_{12}EO_6$*: 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 maternal toxicity were determined to be 50 and 100 mg/kg/day, respectively, according to HERA, with limited study details reported. HERA reported a developmental NOAEL of > 50 mg/kg/day, without describing the basis of this determination. *Due to the limited information provided in this study record, ToxServices was unable to identify a NOAEL or LOAEL for developmental toxicity.*
- HERA concluded that alcohol ethoxylates are not developmental toxicants at non-maternally toxic doses.

- Based on the weight of evidence, a score of Moderate was assigned. In oral studies with alcohol ethoxylate surrogates, reduced pup body weight was reported at maternally toxic doses in rats, which may be nonspecific developmental effects due to maternal toxicity. Information provided in the rabbit study is too limited to determine the relationship between maternal toxicity and developmental toxicity.

Endocrine Activity (E) Score (H, M, or L): DG
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Data Gap for endocrine activity based on the lack of data identified for this endpoint.

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

Group II and II* Human Health Effects (Group II and II* Human)
Note: Group II and Group II* endpoints are distinguished in the v 1.4 Benchmark system (the asterisk indicates repeated exposure). For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints. See GreenScreen® Guidance v1.4, Annex 2 for more details.

Acute Mammalian Toxicity (AT) (Group II) Score (vH, H, M, or L): *M*
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Moderate for acute toxicity based on oral LD_{50} values as low as 1,200 mg/kg for surrogates. 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 low as alcohol ethoxylates with EO between 4 and 6 have a wide range of oral LD_{50} values that correspond to Moderate to Low scores, and no data are available for the target substance.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - GHS – Australia: H302 – Harmful if swallowed
    - GHS – New Zealand: 6.1D (oral) – Acutely toxic (alcohols, C12-14, ethoxylated, >26% in a non-hazardous diluent)
- HERA 2009
  - *Surrogates: AAAs POE (CAS #Multiple)*: In general, the acute toxicity of alcohol ethoxylates 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 alcohol ethoxylates is dependent on the number of EO units in a parabolic fashion but does not depend on the length of the alkyl chain. Alcohol ethoxylates with EO units of greater than 5 and less than 14 have higher acute oral toxicity relative to alcohol ethoxylates with EO units less than 4 or more than 21. Alcohol ethoxylates with EO units greater than 15 had oral LD_{50} values greater than 4,000 mg/kg. Acute oral toxicity is similar between linear and branched alcohol ethoxylates.
    - *Oral:* The acute toxicity of alcohol ethoxylates is associated with the number of EO units rather than the carbon chain lengths.
      - C_xEO_{4-6}: LD_{50} = 1,200 mg/kg to > 10,000 mg/kg
    - *Inhalation:* Data on acute inhalation studies are scarce for alcohol ethoxylates. 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.
      - $C_{9-11}EO_5$: 4h LC_{50} (mist) > 0.22 mg/L (no mortalities or signs of toxicity were observed at 0.22 mg/L, the highest concentration tested).
    - *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, alcohol ethoxylates can be considered to be slightly to practically non-toxic by the dermal route of application.
  - $C_{9\text{-}11}EO_x$: > 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*

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Moderate for systemic toxicity (single dose) based on a lack of systemic toxicity in acute oral, dermal, and inhalation toxicity studies with alcohol ethoxylate surrogates, and a potential of respiratory irritation reactions at high concentrations due to the irritancy of some alcohol ethoxylate category members. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (single dose) when a GHS Category 3 classification is warranted (CPA 2018b). The confidence in the score is reduced as limited data are available, particularly for the inhalation route.

- 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
  - *Oral*
    - *Surrogates: AAAs POE (CAS #Multiple)*: As stated previously, acute oral toxicity of alcohol ethoxylates is dependent on the number of EO units rather than the length of the alkyl chain. Clinical findings in animals following treatment were indicative of gastrointestinal irritation such as ulcerations of the stomach, piloerection, diarrhea, and lethargy, which may be due to administration of a bolus dose. Additionally, lighter animals are more susceptible to acute oral toxicity than heavier animals.
    - *Surrogate: $C_{7\text{-}9}EO_6$:* In a GLP-compliant acute toxicity study conducted according to OECD Guideline 401 that reported an LD_{50} > 2,000 mg/kg in rats, treatment-related clinical signs of toxicity included prone posture, ataxia, and changes in breathing. Clinical signs typically appeared within 4 hours of treatment and animals recovered by day 3. No treatment-related macroscopic changes were found at necropsy.
    - *Surrogate: $C_{11}EO_9$:* In a GLP-compliant acute oral toxicity study conducted according to OECD Guideline 401 that reported an LD_{50} value of 1,100 mg/kg, no treatment-related gross abnormalities were found at necropsy.
  - *Inhalation*
    - *Surrogate: $C_{9\text{-}11}EO_5$:* No mortalities or clinical signs of toxicities were observed in five rats exposed to two different concentrations of the test compound as a mist (mass median diameters of 3.4 and 3.0 μm) (concentrations tested unspecified). Study authors identified a 4h LC_{50} > 0.22 mg/L.
    - *Surrogates: AAAs POE (CAS #Multiple)*: Alcohol ethoxylates are not acutely toxic at saturated vapor concentrations, but acute toxicities were observed when animals were exposed to undiluted test compounds as respirable mists or aerosols. Toxicity effects observed include labored breathing, inactivity, bloody nasal discharge, corneal opacity, lung congestion and mottling, and paleness or congestion of liver, kidneys and adrenals. However, surviving animals had no lasting gross pathology effects. No additional details were provided.
    - *Surrogates: AAAs POE (CAS #Multiple)*: HERA concluded that the respiratory tract irritation potential was not concerning due to the expected low exposure to

aerosolized alcohol ethoxylates during the use of household cleaning products. *ToxServices noted that a GreenScreen® assessment is a hazard assessment and does not consider exposure potential and therefore, ToxServices did not consider HERA's statement to be relevant to the respiratory irritation hazard assessment.*

- *Dermal*
  - *Surrogate: $C_{7\text{-}9}EO_6$:* In a GLP-compliant acute dermal toxicity study, that identified an LD_{50} of > 2,000 mg/kg, no clinical signs of toxicity were found. Additionally, no treatment-related effects were found at necropsy.
  - *Surrogate: $C_{9\text{-}11}EO_6$:* In a GLP-compliant acute dermal toxicity study, male and female rabbits (4/sex/dose) were administered the test substance to abraded skin at a dose of 2,000 mg/kg for 24 hours. There were no mortalities and no clinical signs of toxicity. There were no abnormalities observed at necropsy. An LD_{50} of >2,000 mg/kg was established.
  - *Surrogate: $C_{12\text{-}14}EO_6$:* In a GLP-compliant acute dermal toxicity study according to OECD Guideline 402, male and female rats (5/sex/dose) were administered the test substance at a dose of 2,000 mg/kg. There were no deaths or signs of toxicity observed. An LD_{50} of >2,000 mg/kg was established.
  - *Surrogate: $C_{12\text{-}15}EO_7$:* In a GLP-compliant acute dermal toxicity study, male and female rats (number/sex/dose not specified) were administered the test substance at a dose of 2,000 mg/kg. The only signs of toxicity reported were wet appearance of the fur and inflammation of the treated site. An LD_{50} of >2,000 mg/kg was established.

- Based on the weight of evidence, a score of Moderate was assigned. There was no treatment-related systemic toxicity observed in acute oral or dermal toxicity studies with alcohol ethoxylate surrogates. No systemic toxicities were identified in inhalation studies in animals that survived the exposures. Therefore, alcohol ethoxylates are not classified to GHS Category 1 or 2. However, signs of respiratory irritation such as labored breathing, bloody nasal discharge, and lung congestion and mottling were observed in inhalation studies at high mist/aerosol concentrations. In addition, the irritating properties to the skin and eyes (see relevant sections below) suggest that concentrated alcohol ethoxylates may be irritating to the respiratory tract as well. This classifies alcohol ethoxylates to GHS Category 3, and a score of Moderate can be assigned.

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

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) 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 for surrogates. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when no adverse effects are measured below the guidance values of 100 and 200 mg/kg/day in 90 day oral and dermal studies, respectively (CPA 2018). Confidence in the score is high as it is based on experimental data from well conducted studies.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- HERA 2009
  - *Oral*
    - *Surrogate: $C_{16\text{-}18}EO_{10}$:* An OECD Guideline 408 90-day toxicity study was conducted in male and female rats (10/sex/dose, strain not reported). Animals were administered the test substance at 0, 20, 100, and 500, mg/kg/day via oral gavage. Five animals per six from the control, mid and high dose groups were observed for a

28-day recovery period following exposure. The high dose resulted in delayed growth of the male animals and caused damage to forestomach and kidneys in both male and female rats. Inflammatory changes in the forestomach, seen in the animals in the mid dose group (i.e., 100 mg/kg/day) were less obvious and were reversible. These effects were most likely due to the gavage administration of an irritant concentration of the test substance as similar observations were not made in the dietary studies. On the basis of the observations made in this study, a NOAEL of 100 mg/kg/day can be established.

- *Surrogate: C_{10} EO_5:* A 90-day feeding study was conducted in Sprague-Dawley rats. Animals (20 females/dose) were exposed to the test substance at 125, 250 or 500 mg/kg/day. Clinical observations, body weight and food intake were monitored, clinical chemical examinations and histology on major organs were performed. The only treatment-related effect was a slight increase in absolute liver weight and a dose-dependent increase in relative liver weight which reached statistical significance at the high dose. No histopathological findings were noted. Therefore, the liver weight changes were interpreted as adaptive rather than adverse effects. HERA established the NOAEL at 500 mg/kg/day and the NOEL at 250 mg/kg/day based on liver effects.
- *Surrogate: $C_{9\text{-}11}$ EO_6:* A 90-day feeding study was conducted in rats. Animals (12/sex/dose) were exposed to the test substance at 0, 125, 500, 1,000 or 3,000 ppm. Clinical observation, body weight, food consumption, organ weights, histological examination, hematology and clinical chemical examinations were performed. No significant signs of toxicity were observed. HERA identified the NOAEL at 3,000 ppm, which they translated to 150 mg/kg/day.
- *Surrogate: $C_{9\text{-}11}$ EO_8:* A 90-day feeding study was conducted in Charles River rats. Animals (20/sex/dose) were exposed to the test substance at 0.04, 0.2, or 1.0%. Clinical observation, mortality, ophthalmology, organ weights and histological examination were performed. Statistically significant decrease in body weight gain was found in both sexes at the high dose and a non-significant decrease was found at the mid dose. Food consumption was also statistically significantly decreased at the high dose for both sexes. The authors attributed the decreased weight gain to poor palatability of the test substance. HERA conservatively established the NOEL at 0.2% (equivalent to 80 mg/kg/day) based on this effect (LOEL = 400 mg/kg/day).
- *Surrogate: $C_{12\text{-}15}$ EO_7 and $C_{12\text{-}14}$ EO_7:* Subchronic dietary feeding studies were conducted win male and female Wistar rats that were administered diets containing $C_{12\text{-}15}EO_7$ or $C_{12\text{-}14}EO_7$ 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 $C_{12\text{-}15}EO_7$ and 110 mg/kg/day for $C_{12\text{-}14}EO_7$.
- *Surrogate: $C_{13\text{-}15}$ $EO_{up\ to\ 20}$*: A series of five studies performed with alcohol ethoxylates with C13-15 and up to 20 ethoxy units were performed with male and female rats (10/sex/dose group, strain not specified) administered the alcohol ethoxylates at 100, 250, or 500 mg/kg/day via gavage for 14 days. A treatment-free period of 7 days followed the treatment period. The animals were evaluated for

clinical signs of toxicity, hematology, clinical chemistry, urinalysis, gross pathology, and histopathology. Reversible mild gastric irritation was the only treatment-related effect observed and the study authors identified a NOAEL of 500 mg/kg/day.

- *Surrogate: $C_{14\text{-}15}$ EO_7:* In a 90-day feeding study, male and female Wistar rats (6/dose group) were administered the test substance at 0, 300, 1,000, 3,000 and 10,000 ppm in the diet. Animals were observed for clinical signs, body weight, food intake, clinical chemistry, hematology, organ weight, gross pathology, and histopathology. Decreased mean body weight and food intake was observed in 3,000 ppm females and 10,000 ppm males and females. Changes in organ weights included increased relative liver weight (1,000 ppm females and 3,000 ppm and above males and females), and increase spleen weight (10,000 ppm males). Clinical chemistry revealed significantly higher urea, chloride and potassium levels in 10,000 ppm males, and significantly higher urea, chloride and cholesterol levels in 10,000 ppm females; while hematology revealed increased total leukocytes and lymphocytes (3,000 ppm males and 10,000 ppm males and females) and decreased number of neutrophils, mean cell volume and mean cell hemoglobin (10,000 ppm females). No adverse histopathological changes were observed at any dose level. Based on these observations a conservative NOAEL of 1,000 ppm (reported as equivalent to 50 mg/kg/day) was established. Therefore, the LOAEL is 3,000 ppm (equivalent to 150 mg/kg/day).
- *Surrogate: $C_{14\text{-}15}$ EO_7:* In a 90-day feeding study, male and female albino rats (20/sex/dose) were administered the test substance at 0.1, 0.5 and 1% in the diet. At 28 days, five rats/sex were sacrificed and examined histologically. Remaining animals were observed for clinical signs, body weight, food intake, clinical chemistry, hematology, urinalysis, organ weight, gross pathology, and histopathology. There were no adverse effects reported on any of the evaluated parameters. The authors established the NOAEL at 1%, the highest dose tested (reported as equivalent to 700 and 785 mg/kg/day for males and females, respectively).
- *Surrogate: $C_{12\text{-}14}EO_7$ (linear), $C_{16\text{-}18}EO_{18}$ (linear), and $C_{12\text{-}15}EO_{3\text{-}11}$ (branched)*: A series of oral feeding studies were performed in the same lab with Colworth-Wistar rats (60/group) provided diets containing $C_{12\text{-}14}EO_7$ (linear), $C_{16\text{-}18}EO_{18}$ (linear), or $C_{12\text{-}15}EO_{3\text{-}11}$ (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: $C_{9\text{-}11}$ 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. The available oral and dermal repeated dose toxicity studies with alcohol ethoxylate surrogates of similar carbon chain lengths and/or EO units showed a lack of adverse effects at and below the guidance values of 100 and 200 mg/kg/day, respectively, for a 90-day study.

Neurotoxicity (single dose, N-single) (Group II) Score (vH, H, M, or L): *L*
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Low for neurotoxicity (single dose) based on the lack of clinical signs and gross necropsy findings indicative of neurotoxicity in acute toxicity studies with surrogates. Reversible clinical signs of toxicity such as ataxia were observed in some oral studies. However, they may be due to administration of a bolus dose rather than specific neurotoxicity. GreenScreen® criteria classify chemicals as a Low hazard for single dose neurotoxicity when adequate data are available and they are not classified under GHS for systemic toxicity single exposure based on neurotoxicity (CPA 2018b). Confidence in the score is reduced as limited neurotoxicity endpoints are evaluated in standard acute toxicity tests.

- 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
  - *Oral*
    - *Surrogates: AAAs POE (CAS #Multiple)*: Clinical findings in animals following treatment were indicative of gastrointestinal irritation such as ulcerations of the stomach, piloerection, diarrhea, and lethargy, which may be due to administration of a bolus dose. Additionally, lighter animals are more susceptible to acute oral toxicity than heavier animals.
    - *Surrogate: $C_{7\text{-}9}EO_6$:* In a GLP-compliant acute toxicity study conducted according to OECD Guideline 401 that reported an LD_{50} > 2,000 mg/kg in rats, treatment-related clinical signs of toxicity included prone posture, ataxia, and changes in breathing. Clinical signs typically appeared within 4 hours of treatment and animals recovered by day 3. No treatment-related macroscopic changes were found at necropsy.
    - *Surrogate: $C_{11}EO_9$:* In a GLP-compliant acute oral toxicity study conducted according to OECD Guideline 401 that reported an LD_{50} value of 1,100 mg/kg, no treatment-related gross abnormalities were found at necropsy.
  - *Dermal*
    - *Surrogate: $C_{7\text{-}9}EO_6$:* In a GLP-compliant acute dermal toxicity study, that identified an LD_{50} of > 2,000 mg/kg, no clinical signs of toxicity were found. Additionally, no treatment-related effects were found at necropsy.
    - *Surrogate: $C_{9\text{-}11}EO_6$:* In a GLP-compliant acute dermal toxicity study, male and female rabbits (4/sex/dose) were administered the test substance to abraded skin at a dose of 2,000 mg/kg for 24 hours. There were no clinical signs of toxicity. There were no abnormalities observed at necropsy.
    - *Surrogate: $C_{12\text{-}14}EO_6$:* In a GLP-compliant acute dermal toxicity study according to OECD Guideline 402, male and female rats (5/sex/dose) were administered the test substance at a dose of 2,000 mg/kg. There were no signs of toxicity observed.
    - *Surrogate: $C_{12\text{-}15}EO_7$:* In a GLP-compliant acute dermal toxicity study, male and female rats (number/sex/dose not specified) were administered the test substance at a

dose of 2,000 mg/kg. The only signs of toxicity reported were wet appearance of the fur and inflammation of the treated site.

Neurotoxicity (repeated dose, N-repeated) (Group II*) Score (H, M, or L): DG
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Data Gap for neurotoxicity (repeated dose) based on the lack of data identified for this endpoint.

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

Skin Sensitization (SnS) (Group II*) Score (H, M, or L): L
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Low for skin sensitization based on lack of dermal sensitization reactions in animal and human studies with alcohol ethoxylate surrogates. 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). The confidence in the score is high as data for the strong surrogates are consistent.

- 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
  - *Surrogate: AAAs POE (CAS #Multiple):* Thirty-eight GLP-compliant and non-GLP-compliant skin sensitization studies were identified for alcohol ethoxylates of C9-21 and EO2 – 21 using the Magnusson-Kligman protocol guinea pig maximization test or Buehler protocol in guinea pigs. In most studies the results were negative. Only one study showed weak sensitization potential, which may be attributed to signs of irritation rather than sensitization. It was concluded that AAAs POE are not considered skin sensitizers.
  - *Surrogate: AAAs POE (CAS #Multiple):* A number of human repeated insult patch tests (HRIPT) were conducted on AAAs POE, including $C_{12\text{-}15}EO_7$, $C_{12\text{-}15}EO_9$, $C_{12\text{-}13}EO_{6.5}$, $C_{12\text{-}15}EO_{12}$, $C_{12\text{-}15}EO_{6.5}$, and $C_{12\text{-}15}EO_9$. None of them were concluded to be dermal sensitizers.

Respiratory Sensitization (SnR) (Group II*) Score (H, M, or L): *L*
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Low for respiratory sensitization based on lack of skin sensitization potential and according to ECHA's guidance on respiratory sensitization evaluation (ECHA 2017). GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when adequate data are available and negative and they are not GHS classified (CPA 2018b). The confidence in the score is low as this evaluation does not include non-immunologic mechanisms of respiratory sensitization, and no specific data are available for respiratory sensitization.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2020a
  - Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) does not contain any structural alerts for respiratory sensitization (Appendix D).
- Based on the weight of evidence and guidance from ECHA regarding assessment of respiratory sensitization potential, a score of Low was assigned. The guidance from ECHA states that the mechanisms leading to respiratory sensitization are essentially similar to those leading to skin

sensitization (ECHA 2017). ECHA recommended that if a chemical is not a dermal sensitizer based on high quality data, it is unlikely to be a respiratory sensitizer. ECHA also noted that this rationale does not cover respiratory hypersensitivity caused by non-immunological mechanisms, for which human experience is the main evidence of activity (ECHA 2017). As alcohol ethoxylate surrogates were not sensitizing to the skin (see skin sensitization section above), and a literature search did not find any human evidence of respiratory sensitization by linear (C12 and C14) alkyl alcohols, and as linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) does not contain any structural alerts for respiratory sensitization (OECD 2020a), ethoxylated (6 EO) is not expected to be respiratory sensitizers.

Skin Irritation/Corrosivity (IrS) (Group II) Score (vH, H, M, or L): *L*
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Low for skin irritation/corrosivity based on surrogate data indicating that it is not classifiable under GHS. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate data are available and they are not classified under GHS (CPA 2018b). The confidence in the score is reduced as there were limited details from the surrogate studies that could allow for definitive GHS classification.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - GHS – Australia: H315 – Causes skin irritation
    - GHS – New Zealand: 6.3B – Mildly irritating to the skin (alcohols, C12-14, ethoxylated, >26% in a non-hazardous diluent)
- HERA 2009
  - *Surrogate: AAAs POE (CAS #Multiple):* The skin irritation potential for a range of linear and branched AAAs POE (ranged between C9-11 to C23-25 with 2.5 to 20 ethoxylate units) was tested in numerous studies with rabbits. These studies were conducted with different concentrations ranging from 0.1% to 100%, exposure times ranging from 4 hours to up to 4 weeks and patch conditions such as open applications, semi-occlusive, and fully occlusive conditions. Most of the reported values were from pre-GLP studies. Several studies, however, were in compliance with OECD guidelines and GLP regulations. The results of these studies showed that undiluted alcohol ethoxylates were found to be slightly to severely irritating to skin in rabbits. More concentrated solutions produce more dermal irritation, and alcohol ethoxylates with a lower degree of ethoxylation (i.e., 1-3) are more irritating than those with a higher degree of ethoxylation. No trend in the dermal irritation potential was identified for the length of the alkyl chain. Alcohol ethoxylates are less irritating to human skin than to animal skin, and neat application of a range of alcohol ethoxylates in 4-hour human patch tests indicates that they do not warrant classification on the basis of human data.
  - *Surrogate: $C_{12\text{-}15}\ EO_3$:* In a dermal irritation study conducted according to OECD Guideline 404 under GLP, three rabbits (strain unspecified) were exposed to undiluted test substance on the clipped dorsal skin for 4 hours under semiocclusion. Very slight erythema was observed at 1 hour after patch removal in all rabbits and well-defined erythema were observed at 24 hours in two of the three rabbits. These effects were reversible within 14 days. Desquamation were also observed in all animals on day 8 but was reversible by the end of the observation period. Erythema and edema scores at 24, 48 and 72 hours for individual animal were not report. The primary irritation index (PII) was 1.3, and study authors concluded that the test substance was slightly irritating to the skin.

  - *Surrogate: $C_{13\text{-}15}EO_7$:* In a dermal irritation study in female rabbits (n=3), animals were exposed to 6 doses of neat or a 0.5% solution under occlusive dressing over a 12-day period. Slight to distinct erythema and edema accompanied by cracking and scaling developed in all animals by day seven, and similar levels were seen until the end of the study in animals treated with the neat substance. None of the animals in the 0.5% treatment group showed any signs of dermal irritation at the end of the study.
  - *Surrogate: $C_{9\text{-}11}EO_8$*: In a dermal irritation study in rabbits conducted according to OECD guideline 404, three animals were exposed to the undiluted test substance on the clipped dorsal skin semi-occlusively for 4 hours. Very slight erythema was noted 1 hour after treatment at one of the three dermal test sites. Two sites showed very slight erythema at 24 hours. All the effects were reversible within 7 days. A PII score of 0.6 was calculated, which indicates very slight irritation. A PII of 0.2 was calculated when the test substances were applied at 10% and 25%, indicating minimal irritation potential.
  - *Surrogate: $C_{9\text{-}11}EO_6$*: A GLP-compliant dermal irritation study was conducted in rabbits. The undiluted test material was applied under occlusive conditions on the abraded and intact skin for 24 hours. Severe erythema and edema were observed at 24 and 72 hours. Edema reduced or was absent at day 7, while erythema scores both increased and decreased at some sites compared to 72h observations. The PII score of 5.3 was derived (severely irritating).
  - *Surrogate: $C_{11}EO_9$*: In a dermal irritation study in rabbits conducted according to OECD guideline 404 under GLP, six animals were exposed to the undiluted test substance on the clipped dorsal skin occlusively for 4 hours. Slight erythema and very slight edema were noted in all animals. Desquamation was found on one site at 72 hours which persisted through day 5. All signs of dermal irritation were reversible by day 6. A PII of 1.3 was calculated, which indicates slight irritation potential. Exposure to 1, 10 and 25% of the substance resulted in PII scores of 0, 0.1 and 0.7, respectively, indicating minimal irritation potential.
  - *Surrogate: AAAs POE (CAS #Multiple):* Alcohol ethoxylates have slight to severe irritation potentials in rabbits and rats. In general, undiluted materials were moderate to severe skin irritants, whereas 1% aqueous solutions were mildly irritating, and 0.1- 0.5% solutions were not irritating. Alcohol ethoxylates with lower degree of ethoxylation (i.e. 1-3) were more irritating than those with higher degree of ethoxylation (>4).
- CETOX 2010
  - *Surrogate: AAAs POE (CAS #Multiple):* The skin irritating potential of alcohol ethoxylates generally decreases with increasing level of ethoxylation.
- In summary, dermal exposure to alcohol ethoxylate surrogates may cause severe skin irritation; however, details are insufficient for these studies to allow for classification under GHS criteria (UN 2017). HERA (2009) reports that alcohol ethoxylates have slight to severe irritation potentials in rabbits. Additionally, more concentrated solutions produce more dermal irritation, and alcohol ethoxylates with a lower degree of ethoxylation (i.e., 1-3) are more irritating than those with a higher degree of ethoxylation. Among the studies described above, undiluted $C_{9\text{-}11}EO_6$ caused severe skin irritation in rabbits. However, exposure duration in this study is 24 hours, longer than 4 hours specified in current OECD Guideline 404. Therefore, ToxServices did not weigh this study heavily. Surrogate $C_{12\text{-}15}EO_3$ (undiluted) was slightly irritating to the rabbit skin in a standard 4-hour skin irritation study. Although specific erythema and edema scores were not reported, the term "slightly irritating" seems to indicate that the extent of irritation is lower than "mild" (GHS Category 3), and the substance was not classified under GHS for this endpoint. Since alcohol ethoxylates with higher EO units are less irritating, it is reasonable to deduce that the target

substance $C_{12-14}EO_6$ is less irritating than $C_{12-15}EO_3$, and hence, it is unlikely to be classifiable under GHS.

Eye Irritation/Corrosivity (IrE) (Group II) Score (vH, H, M, or L): *M*
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Moderate for eye irritation/corrosivity based on moderate eye irritation observed with a close surrogate $C_{12-14}EO_6$. GreenScreen® criteria classify chemicals as a Moderate hazard for eye irritation/corrosivity when they are classified to GHS Category 2B (CPA 2018b). The confidence in the score was reduced as limited details were available for the critical study for definitive GHS classification, no structural activity relationships were found for this endpoint, and data were inconsistent.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - GHS – Australia: H318 – Causes serious eye damage
    - GHS – New Zealand: 6.4A – Irritating to the eye (Cat. 2A) (alcohols, C12-14, ethoxylated, >26% in a non-hazardous diluent)
- HERA 2009
  - *Surrogate: $C_{9-11}EO_6$:* A GLP-compliant eye irritation study in 6 rabbits reported corneal opacities that were not reversible within 14 days for the undiluted test material. An overall eye irritation index (EII) of 41.3 was calculated, indicating moderate to severe irritation potential.
  - *Surrogate: $C_{12-15}EO_{11}$:* A GLP-compliant eye irritation study in rabbits reported slight to moderate initial pain, slight to moderate redness of the conjunctivae, slight to moderate chemosis, and slight to severe discharge following instillation of undiluted test substance. An EII of 39 was reported and the test substance was considered to be moderately to severely irritating.
  - *Surrogate: $C_{14-15}EO_7$:* In two pre-GLP Draize eye irritation studies, corneal ulcerations were observed in 5 and 3 animals. EIIs of 12.9 and 14.2 were established. Signs of irritation were still visible at the end of the 7 day observation period.
  - *Surrogate: $C_{14-15}EO_{11}$:* A GLP-compliant eye irritation study in 6 rabbits reported moderate initial pain, iritis (cleared by day 7), and permanent vascularization of the cornea following instillation of undiluted test substance into the conjunctival sac of one eye. An EII of 35.2 was reported and the test substance was considered to be moderately to severely irritating.
  - *Surrogate: $C_{12-14}EO_3$, $C_{12-14}EO_6$, $C_{13}EO_{5-6.5}$, $C_{13}EO_6$ and $C_{12-14}EO_{10}$*: In a series of ocular irritation studies conducted according to OECD Guidelines, $C_{12-14}EO_3$, $C_{12-14}EO_6$, $C_{13}EO_{5-6.5}$, $C_{13}EO_6$ and $C_{12-14}EO_{10}$ produced moderate to severe irritation to rabbit eyes, with eye irritation indices ranging from 27.1-44.2. For some compounds ($C_{13}EO_6$, $C_{13}EO_{5-6.5}$, and $C_{12-14}EO_{10}$) effects were still seen after 21 days.
  - *Surrogate: $C_{12-15}EO_n$*: The eye irritation potential for a range of linear and branched alcohol ethoxylates with the structure C12-15AEn, were tested in a series of OECD compliant studies in rabbits. The calculated eye irritation indexes (EII) ranged from 7.6 to 37.8 for linear alcohol ethoxylates and from 1.5 to 48 for branched compounds, indicating that alcohol ethoxylates are mildly to severely irritating to rabbit eyes. In some of the tested alcohol ethoxylates, the eyes of the treated animals recovered a few days after exposure. In others, exposure caused irreversible damages to the eyes. Rinsing the eyes directly after product application with distilled water for 20 to 30 seconds reduced the severity of the effects and only mild irritation effects were observed. The severity of irritation caused by eye exposure to alcohol ethoxylates was concentration dependent. Concentrations of 0.1%

were considered as virtually non-irritating, and concentrations of 1 to 10% ranged from slight to moderately irritating.
    - *Surrogate: AAAs POE (CAS #Multiple):* The eye irritation potential of alcohol ethoxylates ranged from mild to moderate in rabbit studies, while a few alcohol ethoxylates were corrosive. There was no apparent structure activity relationship between irritation potential and the degree of branching, alkyl chain length, or degree of ethoxylation.
- CIR 2012
    - *Surrogate: $C_{12\text{-}14}EO_6$:* Moderately irritating to the eyes of rabbits (undiluted) in a Draize test with the EII of 27.1/110. No additional details available.
- Based on the weight of evidence, a score of Moderate was assigned. Irreversible damage to the eyes of rabbits was seen in ocular irritation studies conducted according to OECD Guidelines with some alcohol ethoxylate surrogates. However, there did not appear to be a structure activity relationship in eye irritation potential. Therefore, ToxServices relied on data on the closest surrogate above, which is $C_{12\text{-}14}EO_6$, almost identical to the target compound except for the unknown degree of branching in the alkyl chain, to score this endpoint. Limited data were reported for a definitive GHS classification. Based on the qualitative description of Moderate irritation, ToxServices classified it to GHS Category 2B (moderate irritation).

Ecotoxicity (Ecotox)

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

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of High for acute aquatic toxicity based on acute aquatic toxicity values as low as 1.2 mg/L. For algae data, GHS criteria prefer data based on growth rate rather than biomass. Therefore, although EC_{50} values based on biomass are less than 1 mg/L, ToxServices did not consider these values in scoring this endpoint. GreenScreen® criteria classify chemicals as a High hazard for acute aquatic toxicity when acute aquatic toxicity values are between 1 and 10 mg/L (CPA 2018b). The confidence in the score is high as it is based on measured data for strong surrogates.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- HERA 2009
    - Aquatic vertebrate: For the tested chemicals below, it is not clear if the compounds are linear or branched. Therefore, ToxServices considered them surrogates.
        - *Surrogate: $C_{12\text{-}14}EO_6$ (mean)*: An LC_{50} of 2.0 mg/L was determined in the aquatic vertebrate (*Brachydanio rerio*, 96-hr).
        - *Surrogate: $C_{12\text{-}14}EO_6$ (mean)*: An LC_{50} of 1.2 mg/L was determined in the aquatic vertebrate (*Cyprinus carpio*, 96-hr).
        - *Surrogate: $C_{12\text{-}14}EO_6$ (mean)*: An LC_{50} of 1.5 mg/L was determined in the aquatic vertebrate (Zebrafish, 96-hr).
    - Aquatic invertebrate: For the tested chemicals below, it is not clear if the compounds are linear or branched. Therefore, ToxServices considered them surrogates.
        - *Surrogate: $C_{12,14}EO_6$ (mean)*: An EC_{50} (immobilization) of 1.2 mg/L was determined in the aquatic invertebrate (*Daphnia magna,* 48-hr).
        - *Surrogate: $C_{12,14}EO_6$ (mean)*: An EC_{50} (immobilization) of 1.4 mg/L was determined in the aquatic invertebrate (*D. magna,* 48-hr).
    - Aquatic plant: For the tested chemicals below, it is not clear if the compounds are linear or branched. Therefore, ToxServices considered them surrogates.

- *Surrogate: $C_{12,14}EO_6$ (mean)*: An E_bC_{50} (biomass) of 0.7 mg/L and an E_rC_{50} (growth rate) of 1.3 mg/L was determined in the aquatic plant (*Scenedesmus subspicatus*, 72-hr).
- *Surrogate: $C_{12,14}EO_6$ (mean)*: An E_bC_{50} (biomass) of 0.92 mg/L and an E_rC_{50} (growth rate) of 1.5 mg/L was determined in the aquatic plant (*S. subspicatus*, exposure period not identified).
- *Surrogate: $C_{12,14}EO_6$ (mean)*: An E_rC_{50} (growth rate) of 3.8 mg/L was determined in the aquatic plant (*Scenedesmus capricornutum*, exposure period not identified).

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): H
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of High for chronic aquatic toxicity based on chronic aquatic toxicity values as low as 0.112 mg/L on surrogates. 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 high as it is based on measured data for strong surrogates.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- HERA 2009
  - Aquatic vertebrate:
    - *Surrogate:$C_{9\text{-}11}EO_6$*: An EC_{10} (survival) of 8.983 mg/L was determined in the aquatic vertebrate (*Lepomis macrochirus)*.
    - *Surrogate: $C_{9\text{-}11}EO_6$*: A NOEC (survival) of 4.35 mg/L was determined in the aquatic vertebrate (*Pimephales promelas)*.
    - *Surrogate: $C_{9\text{-}11}EO_6$*: A NOEC (survival) of 1.0 mg/L was determined in the aquatic vertebrate (*P. promelas)*.
    - *Surrogate: $C_{9\text{-}11}EO_6$*: A NOEC (reproduction) of 0.73 mg/L was determined in the aquatic vertebrate (*P. promelas)*.
    - *Surrogate: $C_{9\text{-}11}EO_6$*: A NOEC (length) of 1.01 mg/L was determined in the aquatic vertebrate (*Pimephales promelas)*.
    - *Surrogate: $C_{12\text{-}13}OE_{6.5}$*: An EC_{10} (survival) of 0.213 mg/L was determined in the aquatic vertebrate (*P. promelas)*.
    - *Surrogate: $C_{12\text{-}13}EO_{6.5}$*: A NOEC (reproduction) of 0.88 mg/L was determined in the aquatic vertebrate (*L. macrochirus)*.
    - *Surrogate: $C_{12\text{-}13}EO_{6.5}$*: An EC_{10} (survival) of 1.748 mg/L was determined in the aquatic vertebrate (*P. promelas)*.
    - *Surrogate: $C_{12\text{-}13}EO_{6.5}$*: A NOEC (survival) of 0.88 mg/L was determined in the aquatic vertebrate (*P. promelas)*.
    - *Surrogate: $C_{14\text{-}15}EO_7$*: A NOEC (survival) of 0.160 mg/L was determined in the aquatic vertebrate (*L. macrochirus)*.
    - *Surrogate: $C_{14\text{-}15}EO_7$*: An EC_{10} (survival) of 0.121 mg/L was determined in the aquatic vertebrate (*P. promelas)*.
    - *Surrogate: $C_{14\text{-}15}EO_7$*: An EC_{10} (survival) of 1.441 mg/L was determined in the aquatic vertebrate (*P. promelas)*.
    - *Surrogate: $C_{14\text{-}15}EO_7$*: A NOEC (survival) of 0.160 mg/L was determined in the aquatic vertebrate (*P. promelas)*.
    - *Surrogate: $C_{14\text{-}15}EO_7$*: A NOEC (survival) of 0.280 mg/L was determined in the aquatic vertebrate (*P. promelas)*.

- Aquatic invertebrate:
  - Surrogate: $C_{12}EO_6$: An EC_{10} (population) of 0.562 mg/L was determined in the aquatic invertebrate (*Brachionus calyciflorus)*.
  - Surrogate: $C_{14\text{-}15}EO_6$: An EC_{10} (reproduction) of 0.368 mg/L was determined in the aquatic invertebrate (*D. magna)*.
  - Surrogate: $C_{14}EO_6$: An EC_{10} (population) of 0.112 mg/L was determined in the aquatic invertebrate (*B. calyciflorus)*.
- Aquatic plant:
  - Surrogate: $C_{12}EO_4$: An EC_{10} (growth rate) of 0.453 mg/L was determined in algae (*S. subspicatus)*.
  - Surrogate: $C_{12\text{-}14}EO_7$: An EC_{10} (growth rate) of 0.137 mg/L was determined in algae (*S. subspicatus)*.
  - Surrogate: $C_{12}EO_8$: An EC_{10} (growth rate) of 0.325 mg/L was determined in algae (*S. subspicatus*).

Environmental Fate (Fate)

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

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Very Low for persistence based on surrogates meeting the 10-day window. GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when they meet the 10-day window (CPA 2018b). The confidence in the score is high as it is based on consistent experimental data on strong surrogates.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- HERA 2009, OECD 2003
  - For technical mixtures, such as surfactants, the 10-day window is not always applicable. This is largely due to the fact that surfactants are multi-component substances that degrade in a step-wise fashion. As a result, they are subject to multiphase kinetics and, therefore, the 10-day window is not appropriate to evaluate the biodegradation potential of surfactants.
- HERA 2009
  - Alcohol ethoxylates with carbon chain lengths ranging from 8 to 15 and containing between 3 and 20 EO units are considered to be readily biodegradable.
  - As a class, alcohol ethoxylates undergo rapid primary and ultimate biodegradation under both laboratory and field conditions. Under aerobic conditions, linear alcohol ethoxylates are generally easily degraded under aerobic conditions.
  - Alcohol ethoxylates ranging from C12 to C15 will generally reach greater than 60% ultimate biodegradation in a standardized ready biodegradability test. However, a reduced biodegradation has been observed after an EO count of 20.
  - Surrogate: $C_{10\text{-}12}EO_6$: An OECD 301B study reported 83% biodegradation after 28 days. No data regarding the 10-day window were available.
- U.S. EPA 2012
  - Surrogate: $C_{9\text{-}11}EO_6$: C9-11 ethoxylated alcohols (CAS #68439-46-3) was readily biodegradable, consistently meeting the 10-day window, in several OECD 301 series tests. No additional details were provided.
  - Surrogate: $C_{12\text{-}15}EO_7$: 12-15 ethoxylated alcohols (7EO) is readily biodegradable, meeting the 10-day window, in OECD 301 series tests. No additional details were provided.

- *Surrogate: $C_{12\text{-}15}EO_9$*: C12-15 ethoxylated alcohols (CAS #68131-39-5) is readily biodegradable, meeting the 10-day window, in OECD 301 series tests. No additional details were provided.
- *Surrogate: $C_{12}EO_{10}$*: A biodegradation test (screening die-away) was conducted according to a "slightly" modified version of OECD Guideline 301E on a C_{12} linear ethoxylated alcohol with an average of 10EO. The test substance was evaluated at a starting concentration of 10 mg/L with activated municipal sewage sludge, and samples were collected on days 1, 2, 3, 5, 7, 9, 12, 16, and 20 of the experiment. Biodegradation was determined via analyses of residual surfactant and the breakdown products polyethylene glycol (PEG) and free fatty alcohols (FFA); ultimate biodegradation was determined based on the assumption that PEG and FFA are the only metabolites of biodegradation. Primary biodegradation reached nearly 98.5% by day 20 of the test (reported by authors as achieving approximately 90% between days 6-12, following a lag period of 6 days). Ultimate biodegradation reached 10% by approximately day 8 of the test. Approximately 70% biodegradation was reached by day 18 (i.e., within a 10-day window), and approximately 75% by day 20. The study was not conducted beyond day 20. The study authors concluded that ethoxylated alcohols are biodegraded by the central fission pathway with formation of short-chained ethoxylates and PEG, with further degradation into short-chained PEG (Szymanski et al 2002). See Appendix E (1) for the biodegradation graph presented by the study authors.
  - ToxServices notes that biodegradation in the standard OECD Guideline 301E test is determined by DOC removal. It is unclear whether analysis of metabolites accurately determines ultimate biodegradation (complete mineralization). Nevertheless, this study is included as part of the weight of evidence as it provides an indication of the biodegradation rate and kinetics of the test substance.
- *Surrogate: $C_{12\text{-}15}EO_9$ (essentially linear)*: A modified Sturm test was conducted according to OECD Guideline 301B on a $C_{12\text{-}15}$ linear ethoxylated alcohol with an average of 9EO. The test substance was evaluated at starting concentrations of 10, 20, and 50 mg/L using activated acclimated[9] domestic sludge inoculum. The test substance reached a total of 64%, 67%, and 79% biodegradation at 10, 20, and 50 mg/L by the conclusion of the 28-day test. For the 20 mg/L test concentration, the 10% level was reached at approximately days 2-3 and the 60% pass level was reached at approximately day 15 (Shell 1991). Therefore, the 10-day window was not met. See Appendix E (2) for the biodegradation graph presented by the study authors.
- *Surrogate: $C_{12\text{-}15}EO_9$ (essentially linear), $C_{14\text{-}15}EO_7$ (essentially linear), $C_{12\text{-}15}EO_7$ (essentially linear)*: BOD tests were conducted on a $C_{12\text{-}15}$ essentially linear ethoxylated alcohol with an average of 9EO, a $C_{14\text{-}15}$ essentially linear ethoxylated alcohol with an average of 7 EO, and a $C_{12\text{-}15}$ essentially linear ethoxylated alcohol with an average of 7 EO. The test was conducted for 30 days using non-acclimated inoculum. The specific test method was not identified, but the authors reported that a test substance must meet 50% biodegradation to be classified as readily biodegradable according to OECD. All three test substances reached 10% biodegradation at approximately day 4. Approximate biodegradation levels at 5, 10, 15, 20, 25, and 30 days (graphs presented in Appendix E (3 and 4)) were:

[9] It is unclear whether the acclimation corresponds to pre-conditioning, as recommended in the OECD 301 guidelines, or pre-adaptation, which is not permitted under OECD 301 guidelines. Although acclimation most commonly refers to adaptation, later in the test report, the authors specify that adapted sludge (described as inoculum adapted to increasing concentrations of the test substance) was used for a separate simulation test. Therefore, the definition of "acclimated" for the modified Sturm test is unclear.

        - $C_{12-15}EO_9$ (linear): 22%, 50%, 68%, 80%, 85%, and 88%, respectively
        - $C_{14-15}EO_7$ (linear): 23%, 28%, 58%, 68%, 75%, 83%, respectively
        - $C_{12-15}EO_7$ (linear): 30%, 68%, 75%, 82%, 88%, 92%, respectively (Shell 1991)
            - Although it is unclear that this test corresponds to any of the current OECD Guidelines, it was included as supporting data regarding biodegradation rate and kinetics.
    - *Surrogate: $C_{12-14}EO_4$ (linear), $C_{12-14}EO_{11}$ (linear), $C_{16-15}EO_6$*: Ethoxylated alcohols: A biodegradation screening test (OECD 301E) was conducted on C_{12-14} linear ethoxylated alcohols with an average of 4 and 11 EO and C_{16-18} linear ethoxylated alcohols with an average of 5EO. The test substances were tested at concentrations of 5, 25, and 50 mg/L ($C_{12-14}EO_{11}$ was also tested at 15 and 20 mg/L) using activated sewage inoculum. Biodegradation was determined by colorimetric analysis of surfactant levels by spectrophotometry. Biodegradation results (estimated from graphs) for each compound at each concentration are summarized below (Jurado Alameda et al. 2007).
        - $C_{12-14}EO_4$ (linear) (Appendix E (5))
            - 5 mg/L: 10% after 1 day and 70% after 2 days (meets 10-day window)
            - 25 mg/L: 10% after 1 day and 70% after 3 days (meets 10-day window)
            - 50 mg/L: 10% after 4 days and 60% after 16 days (does not meet 10-day window)
        - $C_{12-14}EO_{11}$ (linear) (Appendix E (6))
            - 5-25 mg/L: 10% after 1 day and 70% after 2 days (meets 10-day window)
            - 50 mg/L: 10% after 2 days and 70% after 6 days (meets 10-day window)
        - $C_{16-18}EO_6$ (linear) (Appendix E (7))
            - 5 mg/L: 10% after 1-2 days and 70% after 1-2 days (meets 10-day window)
            - 25 mg/L: 10% after 1-2 days and 70% after 1-2 days (meets 10-day window)
            - 50 mg/L 10% after 2 days and 70% after 4 days (meets 10-day window)
                - ToxServices notes that biodegradation in the standard OECD Guideline 301E test is determined by DOC removal. Therefore, this study indicates primary biodegradation rather than complete mineralization. Nevertheless, this study is included as part of the weight of evidence as it provides an indication of the biodegradation rate and kinetics of the test substance.
    - *Surrogate: $C_{12-14}EO_{11}$ (linear)*: A biodegradation screening test (OECD 301E) was conducted by the authors that conducted the study described above on C12-14 linear ethoxylated alcohols with an average of 11EO. In addition to primary biodegradation, the authors reported on results of a confirmatory test (also conducted according to OECD Guideline 301E) performed over 21 days, which also included daily evaluations of COD and DOC, and determination of percent mineralization. Although detailed results were not presented for DOC, which is the endpoint of interest for the OECD Guideline 301E test, the authors reported that the substance reached greater than 90% biodegradation after "a few days from the start", which indicates that it met the 10-day window (Jurado et al. 2013).
    - *Surrogate: $C_{9-11}EO_6$ (linear)*: A C_{9-11} linear ethoxylated alcohol with 6EO (CAS #68439-46-3) is readily biodegradable as defined by OECD (i.e., meeting the 10-day window). In a closed bottle test conducted according to U.S. EPA methods (Evonik 2017), the test substance (Tomadol 91-6) reached the 10% level after 5 days and reached 70% on days 14-15. See Appendix E(8) for biodegradation graph.
- Based on the weight of evidence, a score of Very Low was assigned. HERA reports that alcohol ethoxylates are readily biodegradable, but notes that the 10-day window is not applicable. Based on

the measured biodegradation data demonstrating that the pass level was reached within 28 days for most alcohol ethoxylates in ready biodegradability tests evaluated by HERA, which is equivalent to be "rapidly degradable" under GHS, and warrants a score of Low. However, a Design for the Environment (DfE) alternatives assessment states that the similar compound alcohols $C_{9\text{-}11}EO_6$ is readily biodegradable, consistently meeting the 10-day window. The report also states that the similar compounds alcohols $C_{12\text{-}15}EO_7$ and alcohols $C_{12\text{-}15}EO_9$ meet the 10-day window in OECD Guideline 301 tests. Accordingly, the trade name ingredient linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) is expected to be readily degradable, meeting the 10-day window. The similar compound alcohols $C_{12\text{-}14}EO_{11}$ meets the 10-day window in a ready biodegradation screening test. Although results for one compound, alcohols $C_{12\text{-}15}EO_9$, fell slightly outside the 10-day window (taking approximately 13 days after the lag period to reach the pass level), the majority of studies indicate that ethoxylated alcohols of similar size and degree of ethoxylation as linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) will meet the 10-day window. Supporting studies, including BOD tests on the essentially linear alcohols $C_{12\text{-}15}EO_9$, $C_{14\text{-}15}EO_7$, and $C_{12\text{-}15}EO_7$ and primary biodegradation tests on alcohols $C_{12\text{-}14}EO_4$, $C_{12\text{-}14}EO_{11}$, and $C_{16\text{-}18}EO_6$ and alcohols $C_{12}EO_{10}$ also demonstrate rapid biodegradation. Overall, the weight of evidence supports that linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) will meet the 10-day biodegradation window.

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

Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Low for bioaccumulation based on the most conservative experimental BCF of 237 for a $C_{14}EO_4$ ethoxylated alcohol surrogate. GreenScreen® criteria classify chemicals as a Low hazard for bioaccumulation when the BCF is between 100 and 500 (CPA 2018b). The confidence in the score is reduced because limited experimental details are available and results vary for surrogates. The measured BCFs on surrogates translate to Very Low and Low scores; therefore, there is a chance that the target substance may warrant a lower score for this endpoint if tested in experiments.

- 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
  - *Surrogate: $C_{14}EO_4$*: A BCF of 237 was determined in the fish (Fathead minnow, 54-72 hr).
  - *Surrogate: $C_{12}EO_8$*: A BCF of 12.7 was determined in the fish (Fathead minnow, 54-72 hr).
  - *Surrogate: $C_{13}EO_8$*: A BCF of 29.5-55 was determined in the fish (Fathead minnow, 54-72 hr).
  - *Surrogate: $C_{14}EO_8$*: A BCF of 56.7-135.2 was determined in the fish (Fathead minnow, 54-72 hr).
  - *Surrogate: AAAs POE (CAS #Multiple):* 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.
  - *Surrogate: AAAs POE (CAS #Multiple):* Estimated partition coefficients (log K_{ow}): $C_{11\text{-}15}EO_{0\text{-}20}$: 2.79 – 6.85
  - *Surrogate: AAAs POE (CAS #Multiple):* Alcohol ethoxylates are not bioaccumulative (BCF < 5,000), based on limited available data and QSAR predictions. In addition, fish rapidly metabolize alcohol ethoxylates.
- Based on the weight of evidence, a score of Low was assigned. Although predicted log K_{ow} values for alcohol ethoxylate surrogates as high as 6.85 suggest a very high bioaccumulation potential, measurement and interpretation of the log K_{ow} for a surfactant is challenging (HERA 2009), and alcohol ethoxylates are rapidly metabolized in aquatic organisms and therefore not expected to

bioaccumulate. ToxServices used the highest measured BCF for of 237 for $C_{14}EO_4$ ethoxylated alcohol among the studies described above to evaluate this endpoint.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *L*
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) was assigned a score of Low for reactivity based on its structure indicating that it is not explosive or oxidizing. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when available data indicate that the chemical does not warrant a GHS classification for any of the reactive sub-endpoints (CPA 2018b). The confidence in the score was low as no measured data were identified.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021b
  - *Surrogate: $C_{12-14}EO_{1-2.5}$:* This substance has no chemical groups associated with explosive properties.
  - *Surrogate: $C_{12-14}EO_{1-2.5}$:* This substance is a non-oxidizing liquid.

Flammability (F) Score (vH, H, M, or L): L
Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) 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 is based on measured data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021b
  - *Surrogate: $C_{12-14}EO_{1-2.5}$:* Flash point = 149°C (method not reported)
- GHS criteria define flammable liquids as chemicals with flash points no greater than 93°C (UN 2019). As the surrogate alcohol ethoxylate has a flashpoint greater than 93°C, a score of Low was assigned.

Use of New Approach Methodologies (NAMs)[10] in the Assessment, Including Uncertainty Analyses of Input and Output

The New Approach Methodology (NAM) used in this GreenScreen® includes *in silico* modeling for respiratory sensitization. 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 2020b, OECD 2020b). The expanded application of NAMs greatly amplifies the need to communicate uncertainties associated with their use. As defined by EFSA (2018), uncertainty is "a general term referring to all types of limitations in available knowledge that affect the range and probability of possible answers to an assessment question." The quality, utility, and accuracy of NAM predictions are greatly influenced by two primary types of uncertainties (OECD 2020b):

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

As shown in Table 4, Type I (input data) uncertainties in linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO)'s NAMs dataset include the absence of experimental data for respiratory sensitization. Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO)'s Type II (extrapolation output) uncertainties are that OECD Toolbox only identifies structural alerts, and does not define applicability domains.

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

Uncertainty Analyses (OECD 2020b)		
Type I Uncertainty: Data/Model Input	**Respiratory sensitization**: No experimental data are available.	
Type II Uncertainty: Extrapolation Output	**Respiratory sensitization**: The OECD Toolbox only identifies structural alerts, and does not define applicability domains.	
Endpoint	**NAMs Data Available and Evaluated? (Y/N)**	**Types of NAMs Data (*in silico* modeling/*in vitro* biological profiling/frameworks)**
Carcinogenicity	N	
Mutagenicity	N	
Reproductive toxicity	N	
Developmental toxicity	N	
Endocrine activity	N	
Acute mammalian toxicity	N	
Single exposure systemic toxicity	N	
Repeated exposure systemic toxicity	N	
Single exposure neurotoxicity	N	

[10] 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).

Repeated exposure neurotoxicity	N	
Skin sensitization	N	
Respiratory sensitization	Y	*In silico* modeling: OECD Toolbox structural alerts
Skin irritation	N	
Eye irritation	N	
Acute aquatic toxicity	N	
Chronic aquatic toxicity	N	
Persistence	N	
Bioaccumulation	N	

References

ChemIDplus. 2021. Linear (C12 and C14) alkyl alcohols, ethoxylated (6 EO) (CAS #68439-50-9). United States National Library of Medicine. Available: http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp.

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

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

Cosmetic Ingredient Review (CIR). 2012. Safety assessment of alkyl PEG ethers as used in cosmetics. Int. *J. Toxicol*. 31(5 Suppl):169S-244S.

European Chemicals Agency (ECHA). 2017. Guidance on information requirements and Chemical Safety Assessment. Chapter R.7a: Endpoint specific guidance. Version 6.0. Dated: July 2017. Available: https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf

European Chemicals Agency (ECHA). 2021a. C&L inventory database. Available : https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/122055

European Chemicals Agency (ECHA). 2021b. REACH dossier for alcohols, C12-14, ethoxylated (CAS #68439-50-9). Available : https://echa.europa.eu/registration-dossier/-/registered-dossier/16040/7/2/2

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

Evonik. 2017. Product Guide. Tomadol Ethoxylated Alcohols. Available: https://household-care.evonik.com/product/household-care/downloads/public/evonik%20-%20tomadol%20product%20guide.pdf

Human & Environmental Risk Assessment (HERA). 2009. HERA on ingredients of European household cleaning products. Alcohol ethoxylates. Version 2.0. Available at: http://www.heraproject.com/files/34-F-09%20HERA%20AE%20Report%20Version%202%20-%203%20Sept%2009.pdf.

Jurado Alameda, E., M. Fernandez-Serrano, J. Nunez-Olea, and M. Lechuga. 2007. Primary biodegradation of commercial fatty-alcohol ethoxylated surfactants: characteristic parameters. *J. Surfactants Deterg*.10: 145-153.

Jurado, E., M. Fernandez-Serrano, F. Rios, and M. Lechuga. 2013. Chapter 3. Aerobic biodegradation of surfactants. In Biodegradation-Life of Science. Available:

https://www.intechopen.com/books/biodegradation-life-of-science/aerobic-biodegradation-of-surfactants.

Madden, J.C., S.J. Enoch, A. Paini, and M.T.D. Cronin. "A Review of In Silico Tools as Alternatives to Animal Testing: Principles, Resources, and Applications," *Alt. Lab. Animals* 1-27, (2020). Available: https://journals.sagepub.com/doi/pdf/10.1177/0261192920965977

Organisation for Economic Co-operation and Development (OECD). 2003. Introduction to the OECD Guidelines for Testing of Chemicals Section 3. Available: http://www.oecd.org/chemicalsafety/testing/5598432.pdf

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

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

Pharos. 2021. Pharos Chemical and Material Library Entry for Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO) (CAS #68439-50-9). Available: http://www.pharosproject.net/material/.

Shell Chemical Company. 1991. Technical bulletin-Shell Chemical Company: Influence of hydrotrope type and extent of branching on environmental response factors of nonionic surfactants. Available: https://p2infohouse.org/ref/31/30313.pdf

Szymanski A., E. Bubien, T. Kurosz, A. Wolniewicz, and Z. Lukaszewski. 2002. Biodegradation of fatty alcohol ethoxylates under the conditions of the die-away test. *Pol. J. Environ. Stud*. 11: 429-433. Available: https://www.pjoes.com/pdf/11.4/429-433.pdf

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

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

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

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

United States Environmental Protection Agency (U.S. EPA). 2009. Alkyl Alcohol Alkoxylates (AAA - JITF CST 1 Inert Ingredient). Human Health Risk Assessment to Support Proposed Exemption from the Requirement of a Tolerance When Used as an Inert Ingredient in Pesticide Formulations. Available: https://www.regulations.gov/document?D=EPA-HQ-OPP-2009-0145-0004

United States Environmental Protection Agency (U.S. EPA). 2012. DfE Alternatives Assessment for Nonylphenol Ethoxylates. Dated May 2012. Available: https://www.epa.gov/sites/production/files/2014-06/documents/npe_final.pdf

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

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

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

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 Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO) (CAS #68439-50-9)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

GREEN SCREEN FOR SAFER CHEMICALS

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	Llinear (C12 and C14) alkyl alcohols, ethoxylated (6EO)	68439-50-9	L	L	L	*M*	DG	*M*	*M*	L	*L*	DG	L	*L*	*L*	*M*	H	H	vL	*L*	*L*	L

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Llinear (C12 and C14) alkyl alcohols,	2

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

Table 6

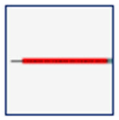
Chemical Name	Final GreenScreen® Benchmark Score
Llinear (C12 and C14) alkyl alcohols,	2

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 Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO) (CAS #68439-50-9)



68439-50-9
C12-14 pareth-7
ALSO CALLED 103819-01-8, 1076240-29-3, 1204655-24-2, 134634-13-2, 141489-71-6, 1459222-40-2, 1802396-38-8, 18925...
View all synonyms (59)

Share Profile

Hazards | Properties | Functional Uses | Resources

GreenScreen Only View

Show PubMed Results | Request Assessment | Add to Comparison

		Group I Human					Group II and II* Human								Ecotox			Fate		Physical		Mult
	GS Score	C	M	R	D	E	AT	ST	ST	N	N	SnS	SnR	IrS	IrE	AA	CA	ATB	P	B	Rx	F	Mult
GreenScreen List Hazards	LT-P1	-	-	-	-	-	H-M	-	-	-	-	-	-	H	vH		-		-	-	-	-	U

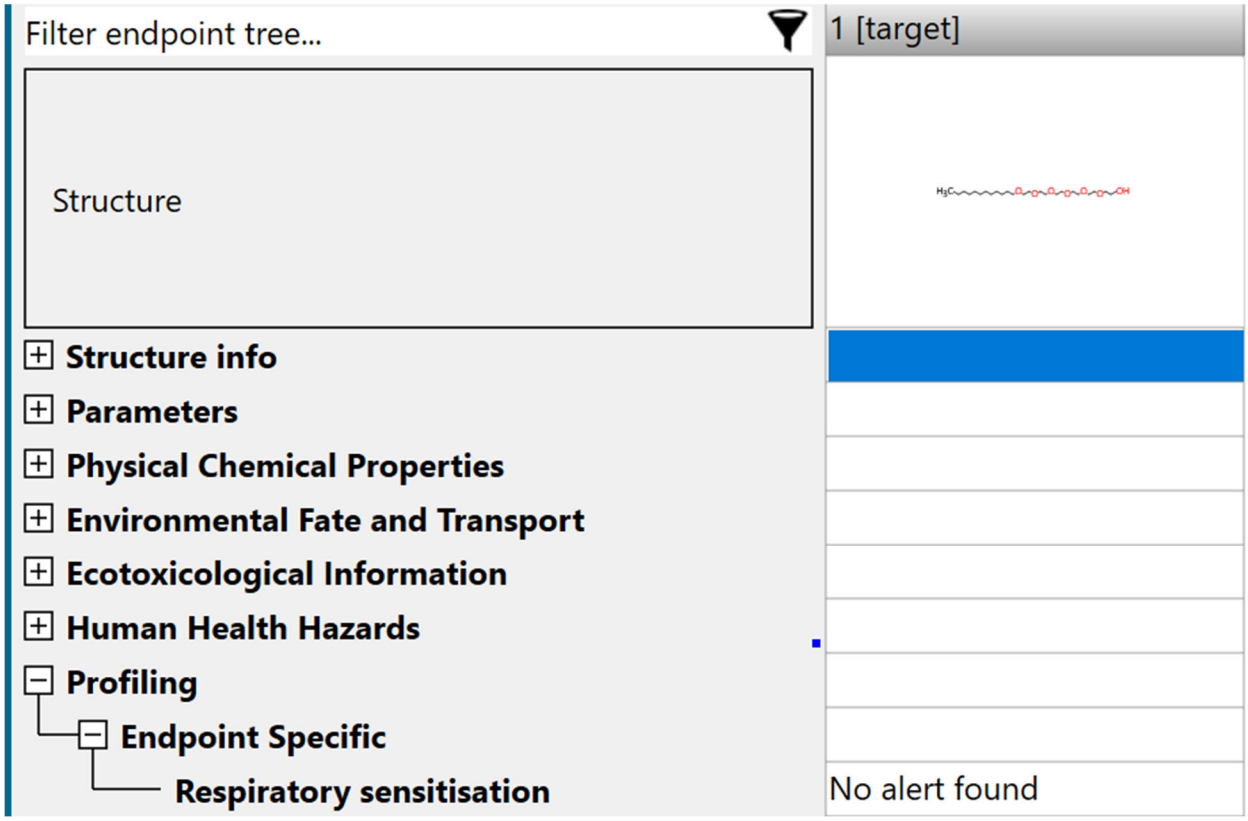
Hazard Lists

Download Lists

ENDPOINT	HAZARD LEVEL	GS SCORE	LIST NAME	HAZARD DESCRIPTION	OTHER LISTS
Acute Mammalian Toxicity	H-M	LT-UNK	GHS - Australia	H302 - Harmful if swallowed	+3
	M	LT-UNK	GHS - New Zealand	6.1D (oral) - Acutely toxic	
	L	LT-UNK	GHS - New Zealand	6.1E (oral) - Acutely toxic	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H302 - Harmful if swallowed (unverified)	
Skin Irritation/Corrosivity	H	LT-UNK	GHS - Australia	H315 - Causes skin irritation	+2
	M	LT-UNK	GHS - New Zealand	6.3B - Mildly irritating to the skin	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H315 - Causes skin irritation (unverified)	

Eye Irritation/Corrosivity	vH	LT-UNK	GHS - Australia	H318 - Causes serious eye damage	+4
	vH	LT-UNK	GHS - New Zealand	8.3A - Corrosive to ocular tissue (Cat. 1)	
	H	LT-UNK	GHS - New Zealand	6.4A - Irritating to the eye (Cat. 2A)	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H318 - Causes serious eye damage (unverified)	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H319 - Causes serious eye irritation (unverified)	
Acute Aquatic Toxicity	pC	NoGS	EU - Manufacturer REACH hazard submissions	H400 - Very toxic to aquatic life (unverified)	
Terrestrial Ecotoxicity	M	NoGS	GHS - New Zealand	9.3B - Ecotoxic to terrestrial vertebrates	
Human and/or Aquatic toxicity and/or Persistence and/or Bioaccumulation	U	LT-P1	German FEA - Substances Hazardous to Waters	Class 2 - Hazard to Waters	
T & P and/or B [(Chronic Aquatic Toxicity and Persistence) or (Acute Aquatic Toxicity and Persistence and/or Bioaccumulation)]	U	LT-P1	GHS - New Zealand	9.1A (algal) - Very ecotoxic in the aquatic environment	+4
	U	LT-P1	GHS - New Zealand	9.1A (other) - Very ecotoxic in the aquatic environment	
	U	LT-UNK	GHS - New Zealand	9.1D (crustacean) - Slightly harmful in the aquatic environment or are otherwise designed for biocidal action	
	U	LT-UNK	GHS - New Zealand	9.1D (fish) - Slightly harmful in the aquatic environment or are otherwise designed for biocidal action	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H412 - Harmful to aquatic life with long lasting effects (unverified)	
Acute aquatic toxicity; Chronic aquatic toxicity	U	LT-UNK	EC - CEPA DSL	Inherently Toxic in the Environment (iTE)	
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)	

APPENDIX D: OECD Toolbox Respiratory Sensitization Modeling Results (OECD 2020a).



APPENDIX E: Biodegradation Test Results for Linear and Essentially Linear Ethoxylated Alcohols

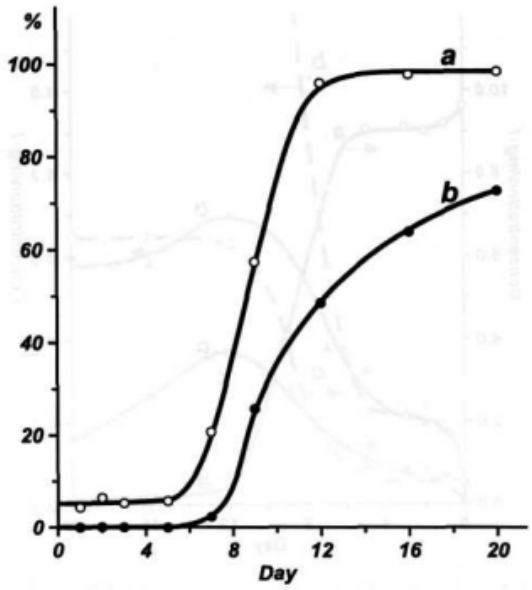
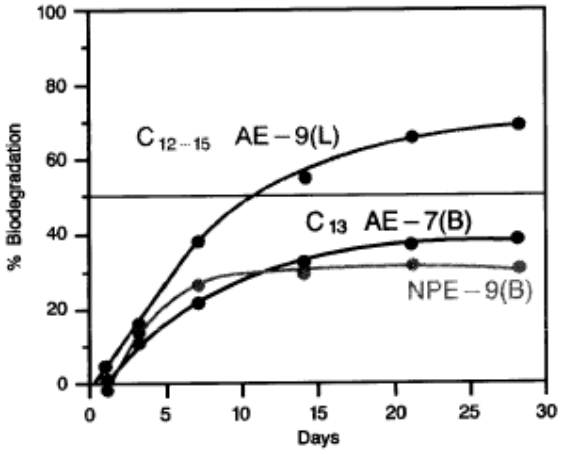


Fig. 2. Primaiy(a) and total(b) biodegradation of surfactant C12E10 during the test.

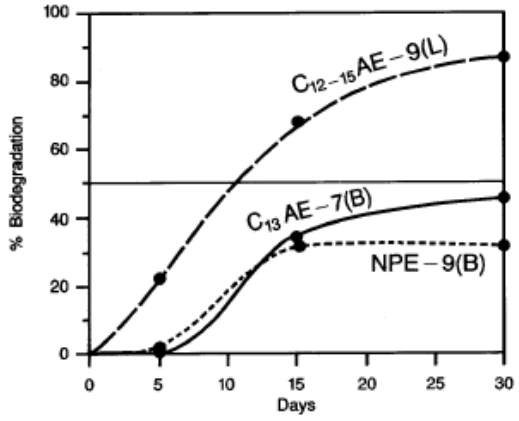
(1) C12; EO10 (Szymanski et al. 2002)

Figure 6/**Effect of hydrophobe on ultimate biodegradation of nonionic surfactants via CO_2 evolution test**



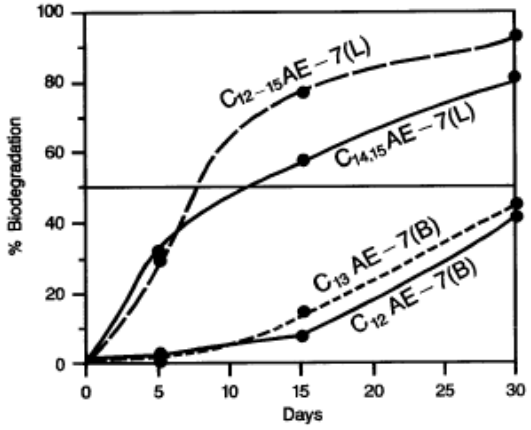
(2) C12-15; EO9 essentially linear (Shell 1991)

Figure 3/**Effect of hydrophobe on biodegradation of nonionic surfactants via BOD test**

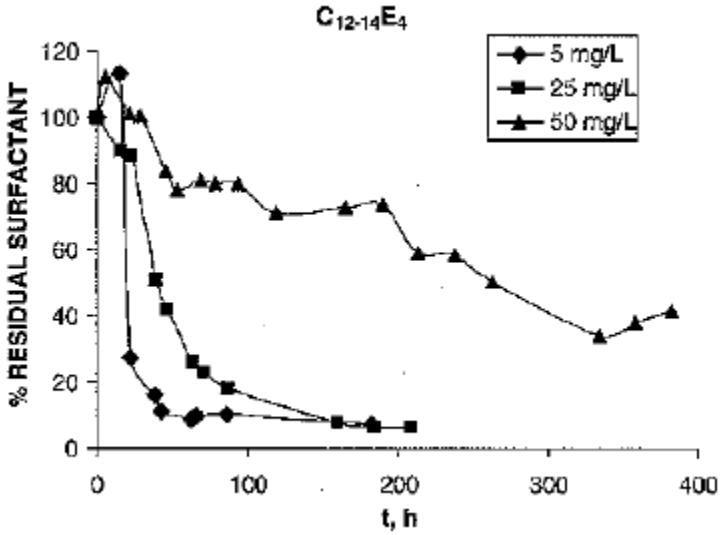


(3) C12-15; EO9 essentially linear (Shell 1991)

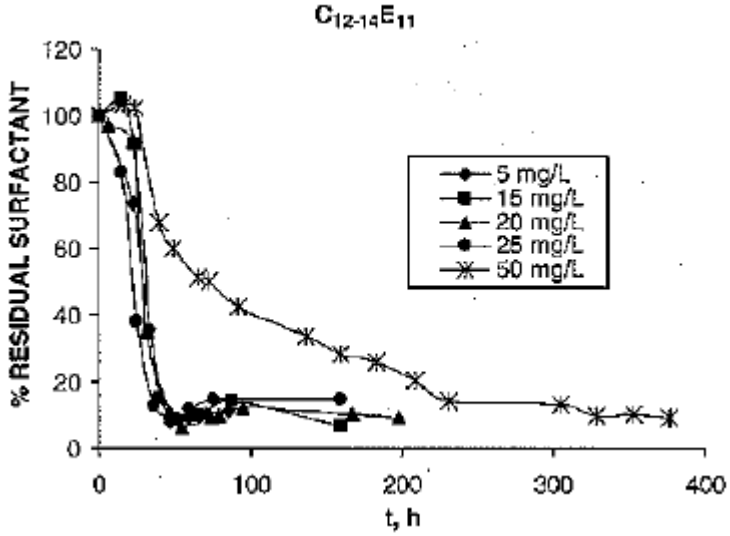
Figure 4/**Effect of hydrophobe chain length on biodegradation of nonionic surfactants via BOD test**



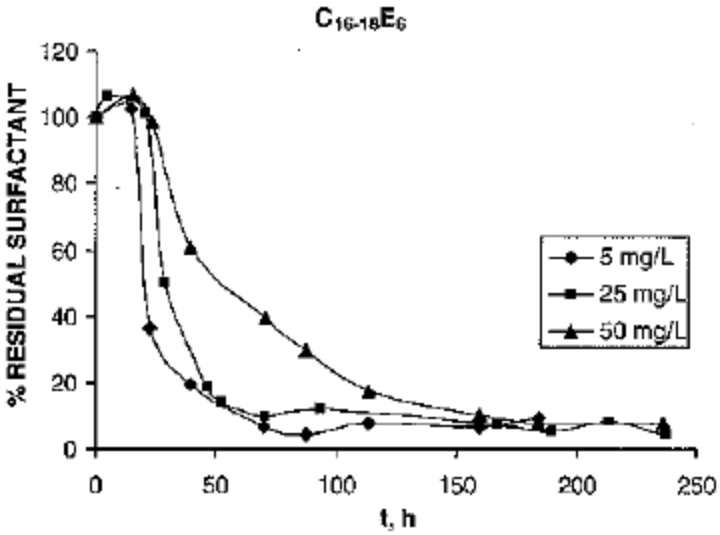
(4) C14-15; EO7, C12-15; EO7 essentially linear (Shell 1991)



(5) C12-14; EO4 (Jurado Alameda 2007)



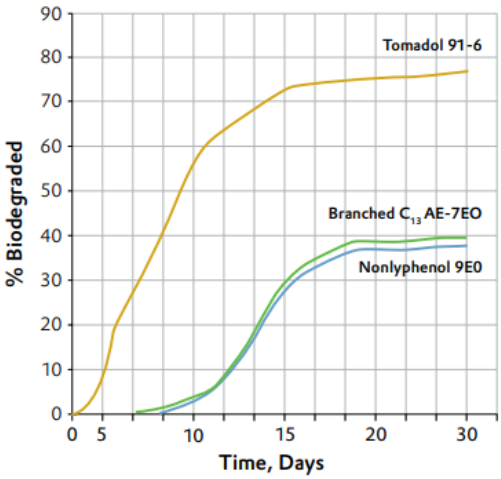
(6) C12-14; EO11 (Jurado Alameda 2007)



(7) C16-18; EO6 (Jurado Alameda 2007)

FIGURE 43

Biodegradation of Tomadol 91-6 and Two Highly Branched Nonionics in Closed Bottle BOD TEST



(8) C9-11; 6EO (Evonik 2017)

Licensed GreenScreen® Profilers

Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO) GreenScreen® Evaluation Prepared by:

SIGNATURE BLOCK

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Toxicologist
ToxServices LLC

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Linear (C12 and C14) Alkyl Alcohols, Ethoxylated (6 EO) GreenScreen® Evaluation QC'd by:

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