D-GLUCOPYRANOSE, OLIGOMERS, DECYL OCTYL GLYCOSIDES (CAS #68515-73-1) GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

ToxServices LLC

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GreenScreen[®] Executive Summary for D-Glucopyranose, Oligomers, Decyl Octyl Glycosides (CAS #68515-73-1)

D-Glucopyranose, oligomers, decyl octyl glycosides is an alkyl polyglycoside obtained by the condensation reaction of octyl and decyl alcohols with a cyclic form of glucose (D-glucopyranose) in the presence of an acid catalyst. The condensation product is a mixture with unknown or variable composition, and the average degree of polymerization ranges from 1 to 3 glucose units.

D-Glucopyranose, oligomers, decyl octyl glycosides is a solid at room temperature but is marketed as an aqueous solution with average water content of 24 - 50%. It is used mainly in cosmetic formulations as a cleansing agent, a foaming agent, and a surfactant. D-Glucopyranose, oligomers, decyl octyl glycosides is highly water soluble, non-volatile, non-reactive and non-flammable.

D-glucopyranose, oligomers, decyl octyl glycosides was assigned a GreenScreen Benchmark[™] Score of 2 ("Use but Search for Safer Substitutes"). This score is based on the following hazard score:

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

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), D-glucopyranose, oligomers, decyl octyl glycosides meets requirements for a GreenScreen Benchmark[™] Score of 2 despite the hazard data gaps. In a worst-case scenario, if D-glucopyranose, oligomers, decyl octyl glycosides were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

New Approach Methodologies (NAMs) used in this GreenScreen[®] include *in vitro* tests for genotoxicity and endocrine activity, and *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 D-glucopyranose, oligomers, decyl octyl glycosides' NAMs dataset include utilizing an unreliable proliferation assay for evaluating estrogenic activity, lack of assays to evaluate other endocrine modalities, and the absence of experimental data and established test methods for respiratory sensitization. D-glucopyranose, oligomers, decyl octyl glycosides' Type II (extrapolation output) uncertainties include the limitations of *in vitro* genotoxicity assays to mimic *in vivo* metabolic conditions, the uncertain predictability of *in vitro* estrogen binding assays of *in vivo* estrogenicity and anti-estrogenicity, and the OECD Toolbox only identifying structural alerts without defining applicability domains. Some of the type I and type II errors can be alleviated by the use of genotoxicity test batteries in combination of *in vivo* data, and ECHA's decision framework to evaluate respiratory sensitization.

(Group	ΗI	uma	n			Gro	up I	I and	I II* I	Ecotox		Fate		Physical				
С	Μ	R	D	Ε	AT	S	Т	1	N	SnS	SnR	IrS	IrE	AA	CA	Р	В	Rx	F
						s	r*	s	r*	*	*								
L	L	L	L	DG	L	L	L	L	DG	L	L	L	vH	Н	Μ	vL	vL	L	L

GreenScreen® Hazard Summary Table for D-Glucopyranose, Oligomers, Decyl Octyl Glycosides

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 D-Glucopyranose, Oligomers, Decyl Octyl Glycosides (CAS #68515-73-1)

Method Version: GreenScreen[®] Version 1.4 Assessment Type¹: Certified Assessor Type: Licensed GreenScreen[®] Profiler

GreenScreen[®] Assessment (v.1.4) Prepared By:

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Expiration Date: April 19, 2026²

<u>Chemical Name:</u> D-Glucopyranose, oligomers, decyl octyl glycosides

CAS Number: 68515-73-1

Chemical Structure(s): D-Glucopyranose, oligomers, decyl octyl glycosides is a substance with unknown or variable composition (ECHA 2021a, ChemIDplus 2021). It is the condensation product of a mixture of octyl and decyl alcohol with a cyclic form of glucose (D-glucopyranose) (CIR 2013). The product mixture has a distribution that can be described by the degree of polymerization (n). The average degree of polymerization ranges from 1 to 3 glucose units as shown below in the representative structure (CIR 2013).



Also called: Caprylyl/capryl oligoglucoside; (C8-C10) alkyl ether of corn sugar (ChemIDplus 2021). D-Glucopyranose, oligomeric, C8-10 glycosides; Alkylpolyglycoside C8 - 10; mixture of di-C8/C10-furanosides and di-C8/C10- glycopyranosides (ECHA 2021a).

Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):

D-Glucopyranose, oligomers, decyl octyl glycosides has limited toxicological data. In its REACH registration dossier data on other alkyl polyglycosides (APGs) such as hexyl D-glucoside (C6 alkyl glycosides, CAS #54549-24-5) and D-glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS

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).

#110615-47-9) were considered to fill the data gaps (ECHA 2021a). All these compounds are mixtures containing D-glucopyranose monomers and oligomers connected with linear fatty alcohols and differ from each other only by the length of the alkyl chains. The Cosmetic Ingredient Review (CIR) Expert Panel reviewed the safety of 19 alkyl polyglucosides for use in cosmetics, including D-glucopyranose, oligomers, decyl octyl glycosides (CIR 2013). Although data gaps exist for many of the alkyl glucosides in this group, these ingredients are expected to have similar toxicological profiles due to their similarities in the structure, physicochemical properties (solids that are marketed in an aqueous solution with an average water content of 24 - 50%) and metabolism (hydrolysis of the β-glycosidic bond to the fatty alcohol and glucose). Therefore, they are expected to have similar toxicity profiles (ECHA 2021a, CIR 2013). Thus, safety data from various glucosides may be used to substantiate the safety of other glucosides of similar chain length. For the carcinogenicity and endocrine activity endpoints, ToxServices used data on the expected metabolites for D-glucopyranose, oligomers, decyl octyl glycosides (CAS # 50-99-7) and octanoic acid (C8, CAS #124-07-2), along with data on the chemical classes (fatty acids and alcohols).



Surrogate: Hexyl D-glucoside (CAS #54549-24-5, representative strucrure, OECD 2020a, ChemIDplus 2021)



n=1 or 2

Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9, representative strucrure, CIR 2013, NICNAS 2009)



Surrogate: D-Glucose (CAS #50-99-7, ChemIDplus 2021)



Surrogate: Octanoic acid (CAS #124-07-2, ChemIDplus 2021)

Identify Applications/Functional Uses: (Pharos 2021, CIR 2013)

- 1. Cleansing agent,
- 2. Foaming agent,
- 3. Surfactant.

Known Impurities³:

According to its REACH registration dossier, D-glucopyranose, oligomers, decyl octyl glycosides may contain the following impurities: sodium p-toluenesulfonic acid (0.7%), and alcohol C8~C18 (0.6%) (ECHA 2021a⁴).

<u>GreenScreen® Summary Rating for D-Glucopyranose, Oligomers, Decyl Octyl Glycosides</u> ^{5,6 7,8}: Dglucopyranose, oligomers, decyl octyl glycosides was assigned a GreenScreen BenchmarkTM Score of 2 ("Use but Search for Safer Substitutes") (CPA 2018b). This score is based on the following hazard score:

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

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), D-glucopyranose, oligomers, decyl octyl glycosides meets requirements for a GreenScreen BenchmarkTM Score of 2 despite the hazard data gaps. In a worst-case scenario, if D-glucopyranose, oligomers, decyl octyl glycosides were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

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

⁴ Information obtained from Study No. 6 under biodegradation section of the REACH registration dossier.

⁵ 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.

⁶ See Appendix A for a glossary of hazard endpoint acronyms.

⁷ For inorganic chemicals only, see GreenScreen[®] Guidance v1.4 Section 12 (Inorganic Chemical Assessment Procedure).

⁸ For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen[®] Guidance v1.4 Annex 2.

Figure 1: GreenScreen[®] Hazard Summary Table for D-Glucopyranose, Oligomers, Decyl Octyl Glycosides

(Group	IH	umai	n			Gro	up I	I and	l II* Human				Ecotox		Fate		Physical	
С	Μ	R	D	Ε	AT	S	Т	I	N	SnS	SnR	IrS	IrE	AA	CA	Р	В	Rx	F
						S	r*	S	r*	*	*								
L	L	L	L	DG	L	L	L	L	DG	L	L	L	vH	Н	М	vL	vL	L	L

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

Environmental Transformation Products

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

Introduction

D-Glucopyranose, oligomers, decyl octyl glycosides is an alkyl polyglycoside mixture obtained by the condensation reaction of octyl and decyl alcohols with a cyclic form of glucose (D-glucopyranose) in the presence of an acid catalyst (CIR 2013). It is used mainly in cosmetic formulations as cleansing agent, a foaming agent, and a surfactant in personal care products (CIR 2013).

ToxServices assessed D-glucopyranose, oligomers, decyl octyl glycosides against GreenScreen[®] Version 1.4 (CPA 2018b) following procedures outlined in ToxServices' SOPs (GreenScreen[®] Hazard Assessment) (ToxServices 2020).

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

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

D-Glucopyranose, oligomers, decyl octyl glycosides is listed on the SCIL as an acceptable surfactant with a full green circle.

GreenScreen® List Translator Screening Results

The GreenScreen[®] List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen Benchmark[™] 1 chemicals (CPA 2018b). Pharos (Pharos 2021) is an online list-searching tool that is used to screen chemicals against all of the lists in the List Translator electronically. ToxServices also checks the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b),⁹ which are not considered GreenScreen[®] Specified Lists but are additional information

⁹ DOT lists are not required lists for GreenScreen[®] List Translator v1.4. They are reference lists only.

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 D-glucopyranose, oligomers, decyl octyl glycosides can be found in Appendix C.

- D-Glucopyranose, oligomers, decyl octyl glycosides is an LT-UNK chemical when screened using Pharos, and therefore a full GreenScreen[®] is required.
- D-Glucopyranose, oligomers, decyl octyl glycosides is not listed on the U.S. DOT list.
- D-Glucopyranose, oligomers, decyl octyl glycosides is on the following list for multiple endpoints.
 - German FEA Substances Hazardous to Waters Class 1 Low Hazard to Waters.
- Specified lists for single endpoints are reported in individual hazard endpoints in the hazard assessment section below.

Hazard Statement and Occupational Control

D-Glucopyranose, oligomers, decyl octyl glycosides is associated with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statement of H318 as shown in Table 1, identified by the majority of notifiers in the European Chemicals Agency (ECHA) classification and labeling inventory (C&L) and in its REACH registration dossier (ECHA 2021a,b). General personal protective equipment (PPE) recommendations are presented in Table 2, below. No occupational exposure limits (OEH) were identified.

Table 1: GHS H Statements for D-Glucopyranose, Oligomers, Decyl Octyl Glycosides (CAS)								
#68515-73-1) (ECHA2021a,b, Pharos 2021)								
H Statement	H Statement Details							
H318	Causes serious eye damage							

Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for D-Glucopyranose, Oligomers, Decyl Octyl Glycosides (CAS #68515-73-1)							
Personal Protective Equipment (PPE)	Reference	Occupational Exposure Limits (OEL)	Reference				
Wear respiratory protection if ventilation is inadequate. Wear suitable chemical resistant safety gloves such as nitrile rubber gloves. Wear safety glasses with side-shields.	ECHA 2021a	None identified.	N/A				

Physicochemical Properties of D-Glucopyranose, Oligomers, Decyl Octyl Glycosides

No physiochemical properties were identified for D-glucopyranose, oligomers, decyl octyl glycosides. Based on data for a structurally similar compound, D-glucopyranose, oligomeric, C10-16-alkyl glycosides, it is expected to be a solid at room temperature and is generally marketed as an aqueous formulation (average water content 50%). D-Glucopyranose, oligomers, decyl octyl glycosides is unlikely be volatile based on a low vapor pressure for the surrogate and is expected to be very soluble in water. The calculated log K_{ow} value of -0.07, for the surrogate indicates that these compounds (alkyl polyglycosides) are hydrophilic and unlikely to bioaccumulate.

Table 3: Physical and Chemical Properties of D-Glucopyranose, Oligomers, Decyl Octyl								
Glycosides (CAS #68515-73-1)								
Property	Value	Reference						
Molecular formula	(C ₆ H ₁₀ O ₅) ₁₋₃ (CH ₂) ₇₋₉ CH ₄ O (representative structure)	ECHA 2021a						
SMILES Notation	[H]O[C@H]1[C@H](O)[C@@H](O)C(OCC)O[C@@H]1CO (building block)	ECHA 2021a						
Molecular weight	> 292 - < 485	ECHA 2021a						
Physical state	Solid	ECHA 2021a						
Appearance	No data available							
Melting point	> 150°C (surrogate data, OECD Guideline 102)	ECHA 2021a,c						
Boiling point	> 301°C (surrogate data, OECD Guideline 103)	ECHA 2021a,c						
Vapor pressure	<= 0.008 Pa at 20°C (surrogate data, OECD Guideline 104)	ECHA 2021a,c						
Water solubility	> 200 g/L (surrogate data, OECD Guideline 105)	ECHA 2021a,c						
Dissociation constant	Not dissociable based on surrogate data (OECD Guideline 112)	ECHA 2021a,c						
Density/specific gravity	1,160 kg/m ³ at 20°C (EU Method A.3, Relative Density)	ECHA 2021a,c						
Partition coefficient	<pre><= -0.07 at 20°C (calculated from the solubility in water and in n-octanol for the surrogate)</pre>	ECHA 2021a,c						

Toxicokinetics

- Absorption
 - o U.S. FDA 2007, ECHA 2021a
 - Oral: <u>Surrogate: Chemical category alkyl polyglycosides (APGs)</u>: Oral absorption of APGs with different fatty alcohols (C8, Cl2 and C16) is expected to be high. They are readily degraded after oral intake due to the fast hydrolysis of the β-glycosidic bond. Based on the similarity in hydrolysis, APGs containing different carbon chain length of fatty alcohols behave identically after oral intake and transform into sugar and fatty alcohol that are also physiologically occurring and of no toxicological concern.
 - ECHA 2021a, CIR 2013
 - Dermal: In a GLP-compliant *in vitro* skin absorption study conducted according to OECD Guideline 428 using abdomen female human skin, D-glucopyranose, oligomers, decyl octyl glycosides (62.8% purity) was absorbed through the skin at a very slow rate with the mean absorbed fraction of 0.01% (Klimisch 1, reliable without restriction).
- Distribution
 - o ECHA 2021a, U.S. FDA 2007
 - <u>Surrogate: Chemical category alkyl polyglycosides (APGs)</u>: In an *in vivo* toxicokinetic study conducted on three alkyl polyglycosides: octyl glucoside (C8),

> dodecyl maltoside (C12), and hexadecyl glucoside (C16), female NMRI mice were administered the radiolabeled substances by gavage. Two hours after treatment the animals were sacrificed and relevant organs were analyzed to determine distribution in specific organs. Stomach, intestines, liver and kidney showed the highest concentrations of radioactivity for the compounds.

- Metabolism
 - o ECHA 2021a, U.S. FDA 2007
 - <u>Surrogate: Chemical category alkyl polyglycosides (APGs)</u>: APGs undergo stepwise hydrolysis into glucose and fatty alcohols, which are further oxidized to the corresponding fatty acids that are incorporated in the citric acid cycle and partly in normal fat metabolism.
 - <u>Surrogate: Chemical category alkyl polyglycosides (APGs)</u>: In the previously described toxicokinetic study in female NMRI mice, the metabolism of the test substances was evaluated. Analysis showed that the test substances are readily cleaved into glucose and fatty alcohols, which are further oxidized to the corresponding fatty acids and partly incorporated in normal fat metabolism. Octyl glucoside was rapidly transformed into hydrophilic metabolites during intestinal and liver passage, whereas hexadecyl glucoside showed a much greater tendency towards lipophilic metabolism, resulting, e.g., in preferential identification in the liver of radiolabeled palmitoyl glycerides. These findings are underlined by the fact that β -oxidation occurs more easily in in medium-chain fatty acids than in long-chain fatty acids.
- Excretion
 - o ECHA 2021a
 - Surrogate: Chemical category alkyl polyglycosides (APGs): The hydrolysis products of APGs as well as the oxidized metabolites are very polar and will be excreted rapidly via urine. Excretion of APGs is assumed to occur mainly via renal elimination. Tissue accumulation can be excluded.
- In summary, D-glucopyranose, oligomers, decyl octyl glycosides are readily absorbed by oral exposure, but minimally absorbed across the skin. Absorbed fraction is mainly distributed to stomach, intestines, liver and kidney. D-Glucopyranose, oligomers, decyl octyl glycosides are expected to be hydrolyzed rapidly to glucose, decanol and octanol, which are then incorporated into cellular carbohydrate and fatty acid metabolism. Excretion of the parent compound and metabolites mainly occurs through kidney into urine.

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for carcinogenicity based on the Generally Recognized As Safe (GRAS) status for its expected metabolites (D-glucose and octanoic acid) supported by data on the long chain aliphatic alcohols and acids. GreenScreen[®] criteria classify chemicals as a Low hazard for carcinogenicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is low due to lack of reliable measured data.

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

- Screening: Not present on any screening lists for this endpoint.
- U.S. FDA 2020a,b
 - <u>Surrogate: D-Glucose (CAS # 50-99-7)</u>: D-Glucose is GRAS according to the United States Food and Drug Administration (U.S. FDA), indicating it has low toxicity including carcinogenicity.
 - <u>Surrogate: Octanoic acid (CAS #124-07-2)</u>: Octanoic acid is GRAS according to the U.S. FDA, indicating it has low toxicity including carcinogenicity.
- HERA 2002
 - <u>Surrogate: Fatty acids and their salts:</u> The use of fats and oils as controls and vehicles in animal toxicity studies due to their innocuous nature, their GRAS status, and long history of safe use indicate a lack of carcinogenic potential for fatty acids and their salts.
- OECD 2006
 - Surrogate: Long chain aliphatic alcohols (C6-22): In skin painting studies, application of hexanol, octanol, decanol, dodecanol, tetradecanol, hexadecanol, or octadecanol 2-3 times weekly for up to 70 weeks at concentrations above the irritating thresholds did not result in local skin tumor development. Together, the results from *in vitro* and *in vivo* genotoxicity studies and the lack of tumor development in skin painting studies indicate members of this group have low carcinogenicity concern.

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for mutagenicity/genotoxicity based on negative results in *in vitro* and *in vivo* assays for mutagenicity and clastogenicity performed with surrogates. GreenScreen[®] criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when adequate data are available and negative for both gene mutation and chromosomal aberration, and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on measured data of good quality for the target chemical and strong surrogates.

- Authoritative and Screening Lists
 - Authoritative: Not present on any authoritative lists for this endpoint.
 - Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a
 - In vitro: Negative results for mutagenicity were seen in a GLP-compliant mammalian cell gene mutation test conducted according to OECD Guideline 476. Mouse lymphoma L5178Y cells were exposed to D-glucopyranose, oligomers, decyl octyl glycosides (20% in ethanol) at 7.5-1,004µg/ml, with and without metabolic activation. No increase in the mutation frequency was observed in the presence or absence of metabolic activation. The vehicle, untreated negative and positive controls were valid (Klimisch 2, reliable with restrictions).
 - In vitro: <u>Surrogate: Hexyl D-glucoside (CAS #54549-24-5)</u>: Negative results for mutagenicity were obtained in a GLP-compliant bacterial reverse mutation assay conducted according to OECD Guideline 471. Salmonella typhimurium tester strains TA 1535, TA 1537, TA 98 and TA 100, and Escherichia coli WP₂ uvr A were exposed to the test substance (75% purity) in dimethyl sulfoxide (DMSO) at concentrations up to 5,000 µg/plate with and without metabolic activation. No increase in the mutation frequency was observed in the presence or absence of metabolic activation. The vehicle and positive controls were valid (Klimisch 1, reliable without restriction).
 - In vitro: <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9)</u>: Negative results for mutagenicity were obtained in a GLP-compliant bacterial reverse mutation assay conducted according to OECD Guideline 471. *S. typhimurium* tester

strains TA 1535, TA 1537, TA 98 and TA 100 were exposed to the test substance (60% purity) in water at concentrations up to 5,000 μ g/plate with and without metabolic activation. No increase in the mutation frequency was observed in the presence or absence of metabolic activation. The vehicle, untreated negative and positive controls were valid (Klimisch 2, reliable with restrictions).

- In vitro: <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9)</u>: The test substance (purity not reported) was negative for mutagenicity in another GLP-compliant bacterial reverse mutation assay conducted according to OECD Guideline 471 using *S. typhimurium* tester strains TA 1535, TA 1537, TA 98 and TA 100 and *E. coli* WP₂ uvr A at concentrations up to 5,000 µg/plate with and without metabolic activation. No increase in the mutation frequency was observed in the presence or absence of metabolic activation. The vehicle, untreated negative and positive controls were valid (Klimisch 1, reliable without restriction).
- In vitro: <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9)</u>: Negative results for clastogenicity were obtained in a GLP-compliant chromosome aberration test conducted according to OECD 473. Chinese hamster lung fibroblasts (V79) cells were exposed to the test material (50% purity) at 2-80 µg/ml, with and without metabolic activation. No increase in the frequency of chromosome aberrations was observed with treatment in the presence or absence of metabolic activation. The vehicle and positive controls were valid (Klimisch 1, reliable without restriction).
- In vivo: <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9)</u>: In a GLP-compliant micronucleus assay conducted according to OECD Guideline 474, male CD-1 mice (7/dose) were administered the test substance (purity not reported) in water at single doses of 0, 62.5, 125, 250 mg/kg via intraperitoneal injection and were sacrificed after 24 hours (vehicle or 48 hours (high dose). The number of polychromatic erythrocytes was not changed and the test substance was considered not clastogenic in this study. The vehicle and positive controls were valid (Klimisch 2, reliable with restrictions).

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for reproductive toxicity based on a lack of reproductive toxicity in a reproduction/developmental toxicity screening test in rats performed with a surrogate. GreenScreen[®] criteria classify chemicals as a Low hazard for reproductive toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is low as it is based on data from a reproduction toxicity screening test that may not have examined all relevant endpoints.

- Authoritative and Screening Lists
 - Authoritative: Not present on any authoritative lists for this endpoint.
 - Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a,c
 - Oral: <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9)</u>: In a GLP-compliant reproduction/developmental toxicity screening test conducted according to OECD Guideline 421, male and female Sprague-Dawley rats (10/sex/dose) were administered the test substance (purity not reported) in water daily by gavage at doses of 0, 100, 300 or 1,000 mg/kg/day. Male rats were exposed for 42 days and toxicity phase females were exposed for 42-47 days. The parental animals were evaluated for clinical signs of toxicity, body weight, food consumption, testes and epididymis weights, ovarian and uterine content, estrous cycle, reproductive indices (copulation index and fertility index), gross pathology, and histopathology. Offspring were evaluated for survival, mean litter size,

sex ratio, body weight, and external and internal abnormalities. There were no treatment related effects on any of the reproductive parameters measured. Authors assigned a NOAEL of 1,000 mg/kg/day for reproductive toxicity, which was the highest dose tested (Klimisch 2, reliable with restrictions).

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for developmental toxicity based on the absence of adverse developmental effects in a prenatal developmental toxicity study in rats performed with a surrogate. GreenScreen[®] criteria classify chemicals as a Low hazard for developmental toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on measured data of good quality for a strong surrogate.

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a,c
 - Oral: <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9)</u>: In the previously described GLP-compliant reproduction/developmental toxicity screening test conducted according to OECD Guideline 421, male and female Sprague-Dawley rats (10/sex/dose) were administered the test substance (purity not reported) in water daily by gavage at doses of 0, 100, 300 or 1,000 mg/kg/day. Male rats were exposed for 42 days and toxicity phase females were exposed for 42-47 days. There were no treatment-related effects on number of live and dead pups, sex ratio, body weight, or external macroscopic examination. Authors assigned a NOAEL of 1,000 mg/kg/day for developmental toxicity, which was the highest dose tested (Klimisch 2, reliable with restrictions).
 - Oral: <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9)</u>: In a GLP-compliant oral prenatal developmental toxicity study conducted according to OECD Guideline 414, pregnant Sprague Dawley rats (24/dose) were administered the test substance (51% purity) in water via gavage at doses of 0, 100, 300 or 1,000 mg/kg/day on gestation days 6-15 and were sacrificed on gestation day 20. Maternal examinations include clinical signs, food consumption, body weight, ovaries and uterine content (number of fetuses, early and late resorptions, total implantations and corpora lutea, and gravid uterine weights). Fetal examinations include litter size, sex ratio, fetal body weights, external, visceral, and skeletal developmental malformations or variations, and visceral variations. There were no treatment related adverse effects on any of these parameters. The authors identified a NOAEL of 1,000 mg/kg/day for maternal and developmental toxicity, which was the highest dose tested (Klimisch 2, reliable with restrictions).

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Data Gap for endocrine activity. Although its expected metabolites (D-glucose and octanoic acid) have GRAS status, there is no evidence that GRAS evaluations consistently consider endocrine activity. Additionally, although *in vitro* high throughput and *in silico* modeling do not indicate a concern for endocrine effects for the surrogates, no *in vivo* data are available. GreenScreen[®] criteria classify chemicals as a Low hazard for endocrine activity when adequate data are available and negative for estrogen agonism and antagonism, and thyroid activity (CPA 2018b). Therefore, there are insufficient data to assign a Low score.

- 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. FDA 2007, CIR 2013
 - <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9):</u> The test substance (Trade name: Glucopon 600 UP, n = 1.4) was inactive for estrogenic activity when tested in two in *vitro* assays, the MCF-7 proliferation assay (E-screen assay) and the MCF-7 reporter gene assay. No effects were noted in the E-screen assay at concentrations up to 10^5 times higher than the 0.1 nmol positive control. In the gene reporter assay, no concentration-dependent induction of luciferase was noted with the D-glucopyranose, oligomeric, C10-16-alkyl glycosides at concentrations up to 100,000 times higher than the positive control. Based on this, it was concluded that the test substance is unlikely to act as an endocrine modulator for the estrogen pathway.
- U.S. FDA 2020a,b
 - Surrogate: D-Glucose (CAS #50-99-7): D-Glucose is GRAS according to the U.S. FDA.
 - Surrogate: Octanoic acid (CAS #124-07-2): Octanoic acid is GRAS according to the U.S. FDA.
- U.S. EPA 2021
 - <u>Surrogate: D-Glucose (CAS #50-99-7)</u>: D-Glucose was inactive in 6/6 estrogen receptor (ER) assays, 8/8 androgen receptor (AR) assays, 2/2 steroidogenesis assays, and 6/6 thyroid receptor assays performed as part of the U.S. EPA's Endocrine Disruptor Screening Program (EDSP) in the 21st Century (Appendix D).
 - <u>Surrogate: D-Glucose (CAS #50-99-7)</u>: D-Glucose was predicted to be inactive for estrogen agonism, antagonism and binding according to the CERAPP Potency Level (Consensus) model. It was also predicted to be inactive for androgen receptor agonism, antagonism and binding according to the COMPARA (Consensus) model (Appendix E).
 - Surrogate: Octanoic acid (CAS #124-07-2): Octanoic acid was active in 5/19 ER assays, 0/14 AR assays, 0/2 steroidogenesis assays, and 1/10 thyroid receptor assays performed as part of the U.S. EPA's EDSP in the 21st Century (Appendix F).
 - <u>Surrogate: Octanoic acid (CAS #124-07-2)</u>: Octanoic acid was predicted to be inactive for estrogen agonism, antagonism and binding according to the CERAPP Potency Level (Consensus and From literature) models. It was also predicted to be inactive for androgen receptor agonism, antagonism and binding according to the COMPARA (Consensus) model (Appendix G).

Group II and II* Human Health Effects (Group II and II* Human)

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

Acute Mammalian Toxicity (AT) (Group II) Score (vH, H, M, or L): L

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for acute toxicity based on oral and dermal LD₅₀ values greater than > 2,000 mg/kg in rats and rabbits. GreenScreen[®] criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD₅₀ values are > 2,000 mg/kg and inhalation LC₅₀ is > 5 mg/L/4h (mist/dust/fume) (CPA 2018b). The confidence in the score is high as it is based on measured data of good quality for the target chemical.

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

- o Screening: Not present on any screening lists for this endpoint.
- CIR 2013
 - *Oral*: LD₅₀ >5,000 mg/kg (male/female rats) (test substance is 50% active ingredient and the degree of polymerization (n) is 1.6).
 - Dermal: LD₅₀ > 2,000 mg/kg (male/female rabbits) (test substance is 50% active ingredient and n = 1.6)
- ECHA 2021a
 - Oral: LD₅₀ > 2,000 mg/kg (male/female rats) (OECD Guideline 423 and GLP-compliant) (Klimisch 1, reliable without restriction).
 - *Dermal*: LD₅₀ > 2,000 mg/kg (male/female rabbits) (OECD Guideline 402 and GLP-compliant) (Klimisch 1, reliable without restriction).

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for systemic toxicity (single dose) based on a lack of systemic toxicity in acute oral and dermal toxicity studies at doses of 2,000 mg/kg (the GHS cut-off value for classification). Reduced body weight in one of nine animals and spotty area of hemorrhage in the lung in 5 of 9 animals that survived to the end of the observation period were found in the dermal study at 2,000 mg/kg; however, these may be attributed by bacterial infection which led to the mortality in one animal, and the lack of systemic toxicity in the oral study at the dose of 2,000 mg/kg (oral bioavailability is typically higher than dermal bioavailability) indicate the effects observed in the dermal study may not be treatment related. GreenScreen[®] criteria classify chemicals as a Low hazard for systemic toxicity (single dose) 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 measured data of good quality for the target chemical.

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a
 - Oral: In a GLP-compliant acute oral toxicity assay conducted according to OECD Guideline 423, Sprague-Dawley rats (3/sex/dose) received a single dose of D-glucopyranose, oligomers, decyl octyl glycosides (purity not reported) at 2,000 mg/kg via gavage. Animals were observed for 14 days post dosing. No mortality occurred during the study and no clinical signs of toxicity were observed. Weight gain was normal in all animals and gross pathological examination of the survived animals did not show any findings. The authors identified an oral LD₅₀ of > 2,000 mg/kg (Klimisch 1, reliable without restriction).
 - *Dermal:* In a GLP-compliant dermal acute toxicity study conducted according to OECD Guideline 402, New Zealand white rabbits (5/sex/dose) were administered D-glucopyranose, oligomers, decyl octyl glycosides (purity not reported) dermally at a single dose of 2,000 mg/kg onto clipped intact skin for 24 hours under semi-occlusive condition. Animals were observed for 14 days post dosing. One female died on day 13 due to Tyzzer's disease (i.e., bacterial infection). Treatment caused mild to moderate irritant effects, fecal staining, yellowing around the application site, emaciation (2 animals), nasal discharge (3 animals), and lacrimation. One of 9 surviving animals lost weight and gross pathological examination of the survived animals did not show any findings other than a spotty area of hemorrhage on the lungs in 5 animals. The authors identified a dermal LD₅₀ of > 2,000 mg/kg (Klimisch 1, reliable without restriction).

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for systemic toxicity (repeated dose) based on a lack of systemic toxicity in a 90-day oral repeated dose toxicity stud. GreenScreen[®] criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when animal studies identify oral LOAEL values greater than 100 mg/kg/day in 90-day studies and when they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on measured data of high quality for a strong surrogate.

- Authoritative and Screening Lists
 - Authoritative: Not present on any authoritative lists for this endpoint.
 - Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a
 - Oral: <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9)</u>: In a GLP-compliant subchronic repeated dose toxicity study conducted according to EU Method B.26, Sprague-Dawley rats (10/sex/dose) were administered oral doses of the test substance (purity not reported) in water at 0, 250, 500, or 1,000 mg/kg/day via gavage for 90 days. The animals were evaluated for clinical signs of toxicity, body weight gain, hematology, clinical chemistry, organ weight, gross pathology, and histopathology. No mortality was seen and there were no treatment related effects on any of the parameters measured. However, local irritation in the stomach was seen in animals at doses of 500 mg/kg and above which was attributed to the irritant properties of the test item. Authors assigned a NOAEL of 1,000 mg/kg/day for systemic toxicity, which was the highest dose tested (Klimisch 1, reliable without restriction). *The dose of 1,000 mg/kg/day is above the GHS Category 2 cut-off value of 100 mg/kg/day for a 90-day study. Therefore, the test substance is not classified per GHS.*
- U.S. FDA 2007
 - Dermal: In a 14-day dermal toxicity study, D-glucopyranose, oligomers, decyl octyl glycosides (60% active substance) was applied to the intact skin of New Zealand white rabbits (number and sex not specified) at doses between 60 and 3,000 mg/kg/day. Treatment caused severe skin irritation as well as several changes in hematological and clinical parameters and testicular atrophy in animals at 1,500 mg/kg/day and above. Minimal to mild skin irritation was seen in treated animals at 540 mg/kg/day whereas no clinical, hematological or organ changes were reported at this dose. At 180 mg/kg/day, there were no treatment related effects and none of the described adverse events were observed. A NOAEL of 540 mg/kg/day was established for systemic toxicity.
- CIR 2013
 - Dermal: In a 14-day toxicity study, New Zealand White rabbits (6/sex/dose) were exposed to D-glucopyranose, oligomers, decyl octyl glycosides (60% active substance) at 0, 900 and 1,800 mg a.i./kg for 6 hours per application for a total of 10 applications under occlusion. One high dose female died during the study as the result of treatment. Clinical signs included ataxia, lethargy and emaciation. Severe dermal irritation developed in both treated groups. Body weights of both treated groups significantly reduced compared to controls. Absolute testes weights significantly reduced in both treated groups. Three of the 6 males each in the low and high dose groups had small testes, and study authors considered this effect to be biologically significant, although not statistically significant. All males at the low dose and 4 males at the high dose exhibited very slight to marked testicular degeneration. Three males each in low and high dose groups had very slight to moderate prostate atrophy and accessory sex glands atrophy. Study authors concluded that all the

observed effects may be attributed to irritation, inflammation and stress of these animals as degenerative changes occur commonly in the testes of normal rabbits. However, study authors also stated that the possibility couldn't be ruled out that the test article specifically caused these effects.

- Dermal: In a 14-day study, New Zealand White rabbits (6 males/dose) were exposed to D-0 glucopyranose, oligomers, decyl octyl glycosides (60% active substance) at 0, 140, 410 and 1,250 mg a.i./kg for 6 hours per application for a total of 10 applications under occlusion. Two high dose animals died prior to the scheduled sacrifice. Severe dermal irritation developed in all treated animals, and even control animals exhibited slight to moderate irritation. Study authors attributed the changes in hematology and clinical chemistry parameters (unspecified) to stress of occlusion procedure, irritation and body weight loss. Mid and high dose groups had decreased absolute testis weights, and a dose dependent body weight loss was found in all treated groups. Relatively small testes were observed in all groups (1, 2, 4 and 6 in control, low, mid and high dose groups). There were treatmentrelated histopathological changes in the testes, epididymides, prostate and vesicular glands at mid and high doses. The NOEL for histopathological changes was 140 mg/kg. One low dose rabbit had the greatest body weight loss, moderate testicular atrophy and a moderate amount of necrotic spermatocytes/spermatids. Study authors stated that the histopathological evaluation of sex organs were complicated by the immaturity of the animals and attributed the changes in testes and accessory sex glands to stress.
- Dermal: In a third 14-day study, New Zealand White rabbits (6 males/dose) were exposed to D-glucopyranose, oligomers, decyl octyl glycosides (60% active substance) at 0, 60, 180 and 540 mg a.i./kg for 6 hours per application for a total of 10 applications under non-occlusive conditions. Skin irritation was developed in all groups and the extent was moderate in high dose group. High dose animals had slight but statistically significant reduction in body weight, and slight and statistically non-significant reduction in absolute testes weights. There were no effects on hematology, clinical chemistry or organ weights. High dose animals exhibited more severe signs of skin irritation upon histopathological examination, including epithelial hyperplasia, hyperkeratosis, congestion and eschar formation. These were not found in other groups. No histopathological abnormalities were found in the testes or accessory sex glands. Study authors identified a systemic toxicity NOEL of 180 mg/kg.
- Based on the weight of evidence, a score of Low was assigned. The subchronic oral study on a surrogate indicates that it is not classifiable under GHS. Several 14-day dermal studies were also identified, and consistently reported skin irritation and male reproductive organ weight changes and/or histopathological changes. However, some of the study authors attributed effects on sex organs to stress. Further, reduced body weight may be secondary to the skin irritation effects. Therefore, a clear systemic effect NOAEL could not be concluded from these studies. The GHS guideline values of 20 and 200 mg/kg/day are multiplied by 6 to 120 and 1,200 mg/kg/day to account for the 14-day exposure period instead of the 90-day duration. Due to the uncertain significance of the effects observed in dermal studies, and the inaccuracy when extrapolating effects from a 14-day study to a subchronic study necessary for GHS classification, ToxServices did not weigh the dermal studies heavily in the overall weight of evidence.

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for neurotoxicity (single dose) based on the lack of neurotoxic effects in acute oral and dermal toxicity studies at the GHS cut-off value of 2,000 mg/kg. GreenScreen[®] criteria classify chemicals as a Low hazard for neurotoxicity (single dose) when adequate negative data are available and they are not GHS classified

(CPA 2018b). The confidence in the score is low as it is based on studies with limited neurotoxicity endpoints examined.

- Authoritative and Screening Lists
 - o Authoritative: Not present on any authoritative lists for this endpoint.
 - o Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a
 - Oral: In the previously described GLP-compliant acute oral toxicity assay conducted according to OECD Guideline 423, Sprague-Dawley rats (3/sex/dose) received a single dose of D-glucopyranose, oligomers, decyl octyl glycosides (purity not reported) at 2,000 mg/kg via gavage. Animals were observed for 14 days post dosing. No mortality occurred during the study and no clinical signs of neurotoxicity were observed. Weight gain was normal in all animals and gross pathological examination of the survived animals did not show any findings. The authors identified an oral LD₅₀ of > 2,000 mg/kg (Klimisch 1, reliable without restriction). Clinical signs of neurotoxicity often evaluated in animal studies include: drowsiness, narcosis, reduced alertness, loss of reflexes, lack of coordination, irritability, fatigue, impaired memory function, deficits in perception and coordination, reaction time, or sleepiness, lethargy, and ataxia. If these effects are not transient in nature, then they shall be considered to support classification for Category 1 or 2 specific target organ toxicity single exposure. As animals in this study did not show any of these signs, ToxServices concluded that D-glucopyranose, oligomers, decyl octyl glycosides was not neurotoxic in this study.
 - Dermal: In the previously described GLP-compliant dermal acute toxicity study conducted according to OECD Guideline 402, New Zealand white rabbits (5/sex/dose) were administered D-glucopyranose, oligomers, decyl octyl glycosides (purity not reported) dermally at a single dose of 2,000 mg/kg onto clipped intact skin for 24 hours under semi-occlusive condition. Animals were observed for 14 days post dosing. One female died due to Tyzzer's disease (i.e., bacterial infection). Treatment caused mild to moderate irritant effects, fecal staining, yellowing around the application site, emaciation (2 animals), nasal discharge (3 animals), and lacrimation. No clinical signs of neurotoxicity were reported. One of 9 surviving animals lost weight and gross pathological examination of the survived animals did not show any findings other than a spotty area of hemorrhage on the lungs in 5 animals. The authors identified a dermal LD₅₀ of > 2,000 mg/kg (Klimisch 1, reliable without restriction).

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Data Gap for neurotoxicity (repeated dose) based on the lack of data identified. The GRAS status for its expected metabolites (D-glucose and octanoic acid) is insufficient to support a Low score as chemicals granted GRAS status may have use level limitations above which adverse effects may still occur.

- 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. FDA 2020a,b
 - Surrogate: D-Glucose (CAS # 50-99-7): D-glucose is GRAS according to the U.S. FDA.
 - Surrogate: Octanoic acid (CAS #124-07-2): Octanoic acid is GRAS according to the U.S. FDA.

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for skin sensitization based on negative results in a mouse local lymph node assay performed with a surrogate. GreenScreen[®] criteria classify chemicals as a Low hazard for skin sensitization 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 experimental data of good quality for strong surrogates.

- Authoritative and Screening Lists
 - o Authoritative: Not present on any authoritative lists for this endpoint.
 - Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a
 - Surrogate: Hexyl D-glucoside (CAS #54549-24-5): The test substance was not sensitizing in a GLP-compliant guinea pig maximization test conducted according to OECD Guideline 406. Male guinea pigs (n = 20) were intradermally induced and challenged with hexyl D-glucoside (purity not reported) undiluted and 75% in distilled water. No positive reactions were observed. The authors concluded that hexyl D-glucoside is not sensitizing under the conditions of the assay (Klimisch 2, reliable with restrictions; due to the study being conducted on a read-across substance).
 - <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9):</u> The test substance was not sensitizing in a GLP-compliant guinea pig maximization test conducted according to EU Method B.6. Female guinea pigs (n = 20) were intradermally induced with 0.1% and epicutaneously with 10% D-glucopyranose, oligomeric, C10-16-alkyl glycosides (purity not reported) in propylene glycol and then challenged with 1.25 and 2.5%. No positive reactions were observed. The authors concluded that D-glucopyranose, oligomeric, C10-16-alkyl glycosides is not sensitizing under the conditions of the assay (Klimisch 2, reliable with restrictions).
 - Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9): The test substance was not sensitizing in a GLP-compliant guinea pig maximization test conducted according to OECD Guideline 406. Female guinea pigs (n = 20) were intradermally induced and epicutaneously challenged with 20% D-glucopyranose, oligomeric, C10-16-alkyl glycosides (50% purity) in water. No positive reactions were observed. The authors concluded that D-glucopyranose, oligomeric, C10-16-alkyl glycosides is not sensitizing under the conditions of the assay (Klimisch 2, reliable with restrictions).
 - Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9): The test substance was not sensitizing in a GLP-compliant guinea pig maximization test conducted according to OECD Guideline 406. Female guinea pigs (n = 20) were intradermally induced with 1% and epicutaneously with 60% D-glucopyranose, oligomeric, C10-16-alkyl glycosides (purity not reported) in physiological saline and then challenged with 10%. No positive reactions were observed. The authors concluded that Dglucopyranose, oligomeric, C10-16-alkyl glycosides is not sensitizing under the conditions of the assay (Klimisch 2, reliable with restrictions).

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for respiratory sensitization based on the absence of structural alerts and guidance from ECHA regarding assessment of respiratory sensitization potential. GreenScreen[®] criteria classify chemicals as a Low hazard for respiratory sensitization when they are not classifiable under GHS in the presence of adequate data

(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
 - Based on its default structure which represents its building blocks (two molecules of Dglucopyranose linked to C9 alcohol), D-glucopyranose, oligomers, decyl octyl glycosides does not contain any structural alerts for respiratory sensitization (Appendix H).
- Based on the weight of evidence and guidance from ECHA regarding assessment of respiratory sensitization potential, a score of Low was assigned. The guidance from ECHA states that the mechanisms leading to respiratory sensitization are essentially similar to those leading to skin sensitization (ECHA 2017). ECHA recommended that if a chemical is not a dermal sensitizer based on high quality data, it is unlikely to be a respiratory sensitizer. ECHA also noted that this rationale does not cover respiratory hypersensitivity caused by non-immunological mechanisms, for which human experience is the main evidence of activity (ECHA 2017). As D-glucopyranose, oligomers, decyl octyl glycosides is not expected to be sensitizing to the skin based on surrogate data (see skin sensitization section above), and a literature search did not find any human evidence of respiratory sensitization by D-glucopyranose, oligomers, decyl octyl glycosides, and as the building blocks for D-glucopyranose, oligomers, decyl octyl glycosides is not expected to be a respiratory sensitization as the building blocks for D-glucopyranose, oligomers, decyl octyl glycosides is not expected to be a respiratory sensitization and structural alerts for respiratory sensitization (OECD 2020a), D-glucopyranose, oligomers, decyl octyl glycosides is not expected to be a respiratory sensitizer.

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for skin irritation/corrosivity based on the results from a dermal irritation test conducted according to OECD Guideline 404 not warranting a GHS classification. GreenScreen[®] criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is low as the study did not test on a neat chemical (100% active ingredient).

- Authoritative and Screening Lists
 - o Authoritative: Not present on any authoritative lists for this endpoint.
 - o Screening: Not present on any screening lists for this endpoint.
- CIR 2013
 - D-Glucopyranose, oligomers, decyl octyl glycosides was reported to be slightly irritating to rabbit skin when tested at a concentration of 30%; no further details were provided. Slight to severe cumulative dermal irritation was observed in three dermal irritation studies in rabbits when a 60% active solution of D-glucopyranose, oligomers, decyl octyl glycosides in distilled water (doses ranging from 0.06 1.8 g active ingredient/kg) was applied openly or under occlusion for 10 consecutive 6-hour applications over a 2-week period.
- ECHA 2021a
 - In a GLP-compliant dermal irritation assay conducted according to OECD Guideline 404, 0.5 mL of D-glucopyranose, oligomers, decyl octyl glycosides (65% purity) was dermally administered to the shaved skin of three New Zealand White rabbits (sex not reported) for 4 hours under semi-occlusive conditions. Animals were monitored for 7 days. The erythema scores at 24, 48, and 72 hours were 0.7 for animal 1, 1.3 for animal 2, and 0.3 for animal 3 with effects being fully reversible within 7 days. The edema scores at 24, 48, and 72 hours were 0 for all animals. Authors concluded that the test substance is not irritating to the skin

> (Klimisch 1, reliable without restriction). According to GHS Criteria, chemicals that are Category 3 (Mild irritant) should have a mean value between 1.5 and 2.3 for erythema/edema in at least 2 of 3 tested animals at 24, 48 and 72 hours or, if reactions are delayed, on 3 consecutive days after the onset of skin reactions. None of the irritation scores in the above study is greater than 1.5. The weight of evidence indicates that Dglucopyranose, oligomers, decyl octyl glycosides is not a dermal irritant.

- Surrogate: Chemical category Alkyl Polyglycosides (APG): Existing data indicate that the skin irritation potential of members of APG increases with increasing chain length. Glycosides with alkyl chain length of C8-10 and branched and linear C9-11-alkyl glycosides have no skin irritating potential whereas C10-16-alkyl glycosides are classified as irritating to the skin when tested in animal tests. Therefore, the breaking point for classification is assumed to be in between these chain lengths.
- Based on the weight of evidence, a score of Low was assigned. D-Glucopyranose, oligomers, decyl octyl glycosides was reported to be severely irritating to the skin at concentration of 60% in repeated dermal toxicity studies. However, slight irritation (not warranting GHS classification) was seen in an acute dermal irritation test conducted according to OECD Guideline 404. According to GHS criteria, the OECD Test Guideline 404 is the currently available internationally validated and accepted animal test for classification for skin corrosive or irritant classifications. Accordingly, ToxServices relied on the results from the OECD Guideline 404 test method and assigned a score of Low. The confidence in the score is low as the study was performed on an aqueous solution containing 65% of D-glucopyranose, oligomers, decyl octyl glycosides and therefore it does not evaluate the irritation potential of the neat chemical (100% active ingredient); as the irritation potential of such compounds is dependent on the concentration.

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Very High for eye irritation/corrosivity based on being severely irritating to the rabbit eye in experimental tests classifying it to GHS Category 1. GreenScreen[®] criteria classify chemicals as a Very High hazard for eye irritation/corrosivity when they are classified to GHS Category 1 (CPA 2018b). The confidence in the score is high as it is based on measured data of high quality for the target chemical.

- Authoritative and Screening Lists
 - Authoritative: Not present on any authoritative lists for this endpoint.
 - Screening: GHS New Zealand 6.4A Irritating to the eye (Cat. 2A)
- CIR 2013
 - D-Glucopyranose, oligomers, decyl octyl glycosides (concentration not specified) was highly irritating in a Hen's Egg Test Chorioallantoic Membrane (HET-CAM) assay.
 - Several ocular irritation tests in rabbits showed that the ocular irritation potential of D-glucopyranose, oligomers, decyl octyl glycosides is concentration-dependent. Undiluted D-glucopyranose was severely irritating to rabbit eyes; however, when the substance was diluted or the eyes were rinsed, the severity and duration of ocular irritation were reduced. The irritation threshold value was 10% for 30% active ingredient and 5% for 60% active ingredient
- ECHA 2021a
 - <u>Surrogate: Chemical category Alkyl Polyglycosides (APG)</u>: Compounds in this category are expected to cause serious damage to eyes.
 - <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9</u>): The test substance was severely irritating to the eye of four rabbits in a GLP-compliant ocular irritation test conducted according to OECD Guideline 405. The test substance (0.1)

gr) was instilled into the conjunctival sac of the left eye of rabbits and animals were observed for 24, 48, 72 hours and 20 days after instillation. The mean cornea scores at 24, 48, and 72 hours were 1 for animal 1, 0 for animal 2, 1 for animal 3, and 0 for animal 4 with effects not being fully reversible within 21 days. The mean chemosis scores at 24, 48, and 72 hours were 1.3 for animal 1, 0.7 for animal 2, 1.7 for animal 3, and 1 for animal 4. Effects were not fully reversible within 21 days. The mean conjunctiva scores at 24, 48, and 72 hours were 3 for animal 1, 1.3 for animal 2, 2.7 for animal 3, and 1.3 for animal 4. Effects were not fully reversible within 21 days. The mean iris scores at 24, 48, and 72 hours were 0.3 for animal 1, 0 for animal 2, 0.7 for animal 3, and 0 for animal 4. Effects resolved within 21 days (Klimisch 2, reliable with restrictions; due to the study being conducted on a read-across substance).

 Authors of REACH dossier classified D-Glucopyranose, oligomers, decyl octyl glycosides to GHS Category 1 for eye irritation with a hazard statement of H318: Causes serious eye damage.

Ecotoxicity (Ecotox)

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of High for acute aquatic toxicity based on an EL_{50} (48-hour) of 7.03 mg/L in marine algae. GreenScreen[®] criteria classify chemicals as a High hazard for acute aquatic toxicity when the most conservative acute aquatic toxicity value is > 1 to 10 mg/L (CPA 2018b). The confidence in the score is high as it is based on measured data of high quality for all three trophic levels for the target chemical.

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a
 - 96-hour LC₅₀ (*Danio rerio*, fish) mortality = 100.81 mg/L nominal (50% purity, GLP-compliant, ISO 7346/1-3 Guideline) (Klimisch 2, reliable with restrictions).
 - 96-hour LC₅₀ (*D. rerio*, fish) mortality = 126 mg/L nominal (70% purity, GLP-compliant, ISO 7346/1-3 Guideline) (Klimisch 2, reliable with restrictions).
 - 96-hour LC₅₀ (*Scophthalmus maximus*, marine fish) mortality = 96.64 mg/L nominal (purity not reported, GLP-compliant, OECD Guideline 203) (Klimisch 2, reliable with restrictions).
 - 96-hour LL₅₀ (*S. maximus*, marine fish) mortality = 541.82 mg/L nominal prepared with water accommodated fraction without analytics (purity not reported, GLP-compliant, OECD Guideline 203) (Klimisch 2, reliable with restrictions).
 - 96-hour NOEC (*Cyprinodon variegatus*, marine fish) mortality = > 21 mg/L nominal (purity not reported, GLP-compliant, OSPARCOM (2005-11) protocol) (Klimisch 2, reliable with restrictions).
 - 48-hour EC₅₀ (*Daphnia magna*, invertebrate) mobility > 100 mg/L nominal (purity not reported, GLP-compliant, OECD Guideline 202) (Klimisch 2, reliable with restrictions).
 - 48-hour EC₅₀ (*Acartia tonsa*, marine invertebrate) mobility = 150.77 mg/L nominal (purity not reported, GLP-compliant and ISO 14669 Guideline) (Klimisch 2, reliable with restrictions).
 - 48-hour EC₅₀ (*A. tonsa*, marine invertebrate) mobility = 31.62 mg/L nominal (purity not reported, GLP-compliant, ISO/PARCOM guidelines for 1990/92) (Klimisch 2, reliable with restrictions).

- 72-hour EC₅₀ (*Desmodesmus subspicatus*, green algae) = 37 mg/L nominal (27.22 mg active ingredient /L) for growth rate and 21 mg active ingredient/L for biomass (56.8% purity, GLP-compliant and DIN 38412 Guideline) (Klimisch 2, reliable with restrictions).
- 72-hour EC₅₀ (*Skeletonema costatum*, marine algae) = 20.71 mg/L nominal (12.43 mg active ingredient /L) for growth rate (60% purity, GLP-compliant and ISO 10253 Guideline) (Klimisch 2, reliable with restrictions).
- 72-hour EL₅₀ (*S. costatum*, marine algae) = 7.03 mg/L nominal for growth rate prepared with water accommodated fraction (purity not reported, GLP-compliant and ISO 10253 Guideline) (Klimisch 2, reliable with restrictions).
- 72-hour EC₅₀ (*Skeletonema sp*, green algae) = 19.82 mg/L nominal for growth rate (purity not reported, GLP-compliant and ISO/PARCOM guidelines for 1990/1) (Klimisch 2, reliable with restrictions).
- U.S. EPA 2012
 - D-Glucopyranose, oligomers, decyl octyl glycosides is assigned a hazard score of Moderate for acute aquatic toxicity based on an experimental 96-hour LC₅₀ of 101 mg/L in fish, an experimental 48-hour EC₅₀ of 20 mg/L in daphnids and an experimental 72-hour EC₅₀ of 47 mg/L in algae.
- Based on the weight of evidence, a score of High was assigned. The acute aquatic toxicity tests for D-glucopyranose, oligomers, decyl octyl glycosides resulted in E(L)C₅₀ values of 27.22 mg/L (active ingredient) in aquatic algae and > 100 mg/L in aquatic invertebrates and fish in the freshwater compartment. In the marine compartment the test substance, D-glucopyranose, oligomers, decyl octyl glycosides, resulted in E(L)C₅₀ values of 7.03 19.82 mg/L in aquatic algae, > 31.62 and 150.77 mg/L in aquatic invertebrates and 96.64 and 541.82 mg/L in marine fish. The most conservative value among these is the EL₅₀ (48 hour) of 7.03 mg/L in marine algae for an aqueous solution containing D-glucopyranose, oligomers, decyl octyl glycosides at unspecified concentration. Therefore, the actual EL₅₀ value for the chemical itself would probably be lower than 7.03 mg/L. This value is within the GreenScreen[®] Guidance values for a High score (> 1 to 10 mg/L). Accordingly, ToxServices relied on the EL₅₀ of 7.03 mg/l in algae and assigned a score of High for this endpoint.

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Moderate for chronic aquatic toxicity based on an experimental NOEC (72-hour) value of 6 mg/L in marine algae and NOEC values of 1.8 - 3.2 mg/L in fish (28-day) and an EC₁₀ value of 1.76 mg/L in daphnia (21-day) for a surrogate. GreenScreen[®] criteria classify chemicals as a Moderate hazard for chronic aquatic toxicity when the chronic aquatic toxicity values are > 1 to 10 mg/L (CPA 2018b). The confidence in the score is high as it is based on measured data of high quality for all three trophic levels for the target chemical and a strong surrogate.

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a
 - 72-hour NOEC (*S. costatum*, marine algae) = 6 mg active ingredient /L for growth rate (60% purity, GLP-compliant and ISO 10253 Guideline) (Klimisch 2, reliable with restrictions).
 - Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9):
 - 28-day NOEC (*D. rerio*, fish) = 1.8 mg active ingredient/L for mortality and 3.2 mg active ingredient /L for growth (50% purity, GLP-compliant and OECD Guideline 204) (Klimisch 2, reliable with restrictions).

- 21-day NOEC (*D. magna*, invertebrate) = 2 mg active ingredient/L for reproduction and 1 mg active ingredient /L for mortality. The LOEC for mortality was 2 mg active ingredient /L and the EC₁₀ was 1.76 mg/L (active ingredient) (50% purity, GLP-compliant and OECD Guideline 202 Part II) (Klimisch 2, reliable with restrictions).
- U.S. EPA 2012
 - D-Glucopyranose, oligomers, decyl octyl glycosides is assigned a hazard score of Moderate for chronic aquatic toxicity based on an experimental 72-hour NOEC of 5.7 mg/L in algae, and an experimental 4-week NOEC of 1.8 mg/L in fish for a surrogate (C12-14 alkyl glycoside), a 21-day NOEC of 1.0 mg/L in daphnia (surrogate) and a 72-hr NOEC of 2.0 mg/L in algae (surrogate).

Environmental Fate (Fate)

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Very Low for persistence based on being readily biodegradable in well conducted studies and meeting the 10-day window in one test. GreenScreen[®] criteria classify chemicals as a Very Low hazard for persistence when data indicate they meet the 10-day window in ready biodegradability tests and mainly partition to water, soil or sediment (CPA 2018b). The confidence in the score is high as it is based on measured data of high quality for the target chemical.

- Authoritative and Screening Lists
 - Authoritative: Not present on any authoritative lists for this endpoint.
 - o Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a
 - D-Glucopyranose, oligomers, decyl octyl glycosides degraded by100% after 28 days in a ready biodegradability test conducted according to OECD Guideline 301E (Modified OECD Screening Test) in which non-adapted activated sludge was exposed to the test substance (purity not reported) for 28 days. Authors concluded that that the test substance was readily biodegradable meeting the 10-day window. No further details were provided (Klimisch 2, reliable with restrictions).
 - In a GLP-compliant ready biodegradability test conducted according to an acceptable Guideline (ECOTOX), non-adapted activated sludge was exposed to D-glucopyranose, oligomers, decyl octyl glycosides (60 % purity) at concentrations of 50 and 100 mg/L for 56 days. A degradation rate of 94.6% was achieved after 56 days. Authors concluded that the test substance is readily biodegradable (Klimisch 1, reliable without restriction).
 - In a GLP-compliant ready biodegradability test conducted according to OECD Guideline 301C (Modified MITI Test (I)), standard activated sludge was exposed to D-glucopyranose, oligomers, decyl octyl glycosides (98.4% purity) at a concentration of 100 mg/L for 14 days. A degradation rate of 73% was achieved after 14 days. Authors concluded that the test substance is readily biodegradable under the test conditions (Klimisch 1, reliable without restriction).
 - In a GLP-compliant ready biodegradability test conducted according to OECD Guideline 301C (Modified MITI Test (I)), non-adapted activated sludge was exposed to D-glucopyranose, oligomers, decyl octyl glycosides (purity not reported) at a concentration of 100 mg/L for 28 days. A degradation rate of 59% was achieved after 28 days. The reference substance degraded by 64% over 28 days. Accordingly, authors concluded that the

test substance is not readily biodegradable under the test conditions (Klimisch 2, reliable with restrictions).

- In a GLP-compliant ready biodegradability test conducted according to OECD Guideline 306 (Ready aerobic degradation in seawater), D-Glucopyranose, oligomers, decyl octyl glycosides (60% purity) degraded in marine water by 55% after 28 days (Klimisch 1, reliable without restriction).
- Nearly 100% of D-Glucopyranose, oligomers, decyl octyl glycosides was degraded in natural river Rhine water in one day.
- U.S. EPA 2012
 - D-Glucopyranose, oligomers, decyl octyl glycosides is assigned a hazard score of very low for persistence based upon experimental data indicating that this material achieves 81-82% degradation after 28 days in an OECD 301D assay and 94% degradation after 28 days in an OECD 301E assay. Further, D-Glucopyranose, oligomers, decyl octyl glycosides met the 10-day window criterion in both tests.
- Based on the weight of evidence, a score of Very Low was assigned. Several studies investigated the biodegradation of D-glucopyranose, oligomers, decyl octyl glycosides. Most of these studies were performed according to OECD guidelines and indicated that D-glucopyranose, oligomers, decyl octyl glycosides was readily biodegradable, and it met the 10-day window in one study. Only one study reported that D-glucopyranose, oligomers, decyl octyl glycosides was not readily biodegradable where 59% degradation was achieved after 28 days. According to the OECD guidance, positive results in ready biodegradability tests are considered valid regardless of negative results, when the scientific quality of the positive study is appropriate (OECD 2001). Therefore, ToxServices relied on the OECD 301E study that reported 100% degradation in 28 days to assign a score of Very Low for this endpoint. This is consistent with the U.S. EPA's conclusion that D-glucopyranose, oligomers, decyl octyl glycosides has a very low score for persistence. While modeling with EPI Suite™ could not be performed to determine environmental distribution as surfactants are outside the applicability domain of the software, the high water solubility and low vapor pressure indicates that the substance is unlikely to mainly partition to the air.

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Very Low for bioaccumulation based on measured log K_{ow} values of 1.72 and -0.07 for its surrogates. GreenScreen[®] criteria classify chemicals as a Very Low hazard for bioaccumulation when BCFs/BAFs are ≤ 100 and log K_{ow} values are ≤ 4 (CPA 2018b). The confidence in the score is high as it was based on measured log K_{ow} values for strong surrogates.

- Authoritative and Screening Lists
 - Authoritative: Not present on any authoritative lists for this endpoint.
 - Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a
 - <u>Surrogate: Hexyl D-glucoside (CAS #54549-24-5)</u>: The test substance has a measured log K_{ow} value of 1.72 at 40°C and pH 6.5 obtained from a GLP-compliant test conducted according to the EU Method A.8 Guideline (HPLC Method) (Klimisch 2, reliable with restrictions; due to the study being conducted on a read-across substance).
 - Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9): The test substance has a log K_{ow} value of < = -0.07 at 20°C calculated from the solubility in water and in n-octanol (Klimisch 2, reliable with restrictions; due to the study being conducted on a read-across substance).

Physical Hazards (Physical)

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for reactivity based on NFPA and HMIS reactivity ratings supported by lack of structural alerts for explosivity. GreenScreen[®] criteria classify chemicals as a Low hazard for reactivity when available data indicate that the chemical does not warrant GHS classification for any of the reactivity sub-endpoints and the chemical is not present on authoritative or screening list (CPA 2018b). The confidence in the score is low due to lack of measured data.

- Authoritative and Screening Lists
 - Authoritative: Not present on any authoritative lists for this endpoint.
 - Screening: Not present on any screening lists for this endpoint.
- No measured data were identified. Therefore, screening procedures for explosivity were used here to estimate the reactivity property of D-glucopyranose, oligomers, decyl octyl glycosides. These procedures are listed in the GHS (UN 2019).
 - Based on the structure of its building blocks, D-glucopyranose, oligomers, decyl octyl glycosides is not considered explosive or self-reactive due to lack of functional groups associated with explosive or self-reactive properties (See Appendix I).
 - Based on the structure of its building blocks, D-glucopyranose, oligomers, decyl octyl glycosides is not considered to have oxidizing properties as it does not contain any structural groups known to be correlated with a tendency to react exothermally with combustible materials.
- Jarchem 2015
 - A safety data sheet for an aqueous solution of D-glucopyranose, oligomers, decyl octyl glycosides (30 50%) has a reactivity rating of 0 from the NFPA and HMIS; which correspond to "Normally stable, even under fire exposure conditions, and is not reactive with water" (NFPA 2017) and "Materials that are normally stable, even under fire conditions, and will not react with water, polymerize, decompose, condense, or self-react. Non-explosives" (ILPI 2020), respectively.

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

D-Glucopyranose, oligomers, decyl octyl glycosides was assigned a score of Low for flammability based on negative results in flammability tests with surrogates. GreenScreen[®] criteria classify chemicals as a Low hazard for flammability 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 measured data of high quality for strong surrogates.

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - Screening: Not present on any screening lists for this endpoint.
- ECHA 2021a
 - Surrogate: Hexyl D-glucoside (CAS #54549-24-5): The test substance (monoglucoside: 58.3%, diglucoside: 18.2%, water: 0.9% and higher oligomers: < 21.2%) is not a flammable solid when tested according to EU Method A.10 (Flammability (Solids)). No ignition and no propagation of combustion occurred (Klimisch 2, reliable with restrictions; due to the study being conducted on a read-across substance).
 - <u>Surrogate: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (CAS #110615-47-9):</u> The test substance (purity not reported) is not a flammable solid when tested according to EU Method A.10 (Flammability (Solids)). No ignition and no propagation of combustion

> occurred (Klimisch 2, reliable with restrictions; due to the study being conducted on a readacross substance).

<u>Use of New Approach Methodologies (NAMs)¹⁰ in the Assessment, Including Uncertainty Analyses of Input and Output</u>

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

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

As shown in Table 4, Type I (input data) uncertainties in D-glucopyranose, oligomers, decyl octyl glycosides' NAMs dataset include utilizing an unreliable proliferation assay for evaluating estrogenic activity, lack of assays to evaluate other endocrine modalities, and the absence of experimental data and established test methods for respiratory sensitization. D-glucopyranose, oligomers, decyl octyl glycosides' Type II (extrapolation output) uncertainties include the limitations of *in vitro* genotoxicity assays to mimic *in vivo* metabolic conditions, the uncertain predictability of *in vitro* estrogen binding assays of *in vivo* estrogenicity and anti-estrogenicity, and the OECD Toolbox only identifying structural alerts without defining applicability domains. Some of the type I and type II errors can be alleviated by the use of genotoxicity test batteries in combination of *in vivo* data, and ECHA's decision framework to evaluate respiratory sensitization.

Table 4: Summary of NAMs Used in the GreenScreen [®] Assessment, Including Uncertainty							
Analyses							
Uncertainty Analyses (OECD 2020b)							
Type I Uncertainty: Data/Model Input	Genotoxicity: No Type I uncertainty is identified on using the <i>in</i> <i>vitro</i> genotoxicity as they are considered relevant (appropriate for the evaluation of the corresponding hazards as recommended in the OECD Guideline), reliable (they have Klimisch scoring of 2 or 1) and adequate (validated methods). Endocrine activity: The <i>in vitro</i> E-screen assay is based on the induction of proliferation, i.e., proliferation in estrogen-responding cells, particularly in the MCF-7 human breast cancer cell line, is used to detect estrogenic activity. However, proliferation assays are not recommended by Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) because cell proliferation can be mediated through pathways other than those involving transcriptional activation of estrogen responsive genes (OECD 2010). No Type I uncertainty is identified on using the other <i>in vitro</i> assay, MCF-7 reporter gene assay, as it is performed						

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).

	according to the OECD Guideline 455. However, data on other						
	endocrine disruption modalities	are needed (androgen, thyroid and					
	steroidogenesis).						
	Respiratory sensitization: No experimental data are available.						
Type II Uncertainty: Extrapolation Output	 Respiratory sensitization: No experimental data are available. Genotoxicity: The bacterial reverse mutation assay (OECD 471) only tests point-mutation inducing activity in non-mammalian cells, and the exogenous metabolic activation system does not entirely mimic <i>in vivo</i> conditions¹¹. The mammalian cell gene mutation assay (OECD 476) only detects gene mutations, and the exogenous metabolic activation system does not entirely mirror <i>in vivo</i> metabolism¹². The <i>in vitro</i> chromosome aberration assay (OECD 473) does not measure aneuploidy and it only measures structural chromosomal aberrations. The exogenous metabolic activation system does not entirely mirror <i>in vivo</i> genotoxicity study was available on a strong surrogate and gave negative results. Accordingly, no Type II uncertainty is identified on using the <i>in vitro</i> assays used in this assessment are appropriate to evaluate the estrogen activity endpoint. However, the predictability of <i>in vitro</i> assays to <i>in vivo</i> situations has not been established. Respiratory sensitization: The OECD Toolbox only identifies structural alerts, and does not define applicability domains. Therefore, there is uncertainty on using the OECD QSAR toolbox 						
	alert is identified. This is because lack of alert might not necessary be due to effect but rather due to the lack of knowledge as there may be other mechanisms not included in the model. For respiratory sensitization, there is still uncertainty regarding the exact underlying mechanisms. In addition, there are no formally recognized and validated animal or <i>in vitro</i> tests and the assessment relies on human						
	evidence or a WoE approach us	ing different types of data. ECHA					
	Guidance regarding the assessm	nent of respiratory sensitization					
	potential along with the OECD	QSAR toolbox were used in a					
	weight of evidence approach.						
Endpoint	NAMs Data Available and Evaluated? (Y/N)	Types of NAMs Data (<i>in silico</i> modeling/ <i>in vitro</i> biological					
	(proming/frameworks)					
Carcinogenicity	N						
Carcinogenicity Mutagenicity	N Y	<i>In vitro</i> data: Bacterial reverse mutation assay/ <i>in vitro</i> gene					

¹¹ https://www.oecd-ilibrary.org/docserver/9789264071247-en.pdf?expires=1614097593&id=id&accname=guest&checksum=89925F80B9F4BD2FFC6E90F94A0EE427 ¹² https://www.oecd-ilibrary.org/docserver/9789264264809-

en.pdf?expires=1614097800&id=id&accname=guest&checksum=C0DE371FB9C5A878E66C9AB7F84E6BBE ¹³ https://www.oecd-ilibrary.org/docserver/9789264264649-

en.pdf?expires=1614098015&id=id&accname=guest&checksum=6A4F9CE52EA974F5A74793DD54D54352

		mutation assay/in vitro
		chromosome aberration assay
Reproductive toxicity	Ν	
Developmental toxicity	N	
Endocrine activity	Y	<i>In vitro</i> data: MCF-7 proliferation assay (E-screen assay) and the MCF-7 reporter gene assay
Acute mammalian toxicity	Ν	
Single exposure systemic toxicity	Ν	
Repeated exposure systemic toxicity	Ν	
Single exposure neurotoxicity	Ν	
Repeated exposure neurotoxicity	Ν	
Skin sensitization	Ν	
Respiratory sensitization	Y	<i>In silico</i> modeling: OECD Toolbox structural alerts/Danish QSAR
Skin irritation	Ν	
Eye irritation	Ν	
Acute aquatic toxicity	Ν	
Chronic aquatic toxicity	Ν	
Persistence	Ν	
Bioaccumulation	Ν	

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<u>APPENDIX A: Hazard Classification Acronyms</u> (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 D-Glucopyranose, Oligomers, Decyl Octyl Glycosides (CAS #68515-73-1)

TX	SERV	ICES								G	FreenSc	reen®	Score I	nspecto	r							
	TOXICOLOGY RISK ASSE	SSMENT CONSULTING	Table 1:	Hazard Ta	ble																	
	-			Gr	oup I Hun	nan			r		Group	II and II*	Human				Eco	otox	Fa	ite	Phys	sical
		ALS N.	Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Svetemie Tovicity				Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
Table 2: Cher	mical Details								S	R *	S	R *	*	*								
Inorganic Chemical?	Chemical Name	CAS#	С	М	R	D	Е	AT	STs	STr	Ns	Nr	SNS*	SNR*	IrS	IrE	AA	СА	Р	В	Rx	F
No	D- Glucopyranose, Oligomers, Decvl	68515-73-1	L	L	L	L	DG	L	L	L	L	DG	L	L	L	vH	н	М	vL	vL	L	L
			Table 3:	Hazard Su	mmary Ta	ble						_	Table 4]			Table 6				
			Bencl	hmark	a	b	c	d	e	f	g		Chemic	al Name	Prelin GreenS Benchma	ninary creen® urk Score		Chemic	al Name	Fi GreenS Benchma	nal creen® urk Score	
				1	No	No	No	No	No				D-Gluco	pyranose,				D-Gluco	pyranose,			
				2	No	No	No	No	No	Yes	No	1	Oligome	rs, Decyl	1	2		Oligome	rs, Decyl		2	
				3	STOP							1	Note: Chemi	cal has not un	dergone a data	ean		After Data ga	ap Assessment			
				4	STOP							1	assessment. N	Not a Final Gre	een Screen™ Sc	ore		Note: No Da GS Benchmar	ta gap Assess k Score is 1.	nent Done if I	Preliminary	
			Table 5:	Data Gap 🛛	Assessme	nt Table										F 1	1					
			Datagap	o Criteria	a	b	c	d	e	f	g	h	i	j	bm4	End Result						
				2	Ves	Ves	Ves	Ves	Ves							2						
				3	105	100	100	105	105							~						
			4	4													1					

APPENDIX C: Pharos Output for D-Glucopyranose, Oligomers, Decyl Octyl Glycosides (CAS #68515-73-1)

Pharos Q Search				Comparisons	Common Products	Discussions 💄 Accoun
68515-73-1 D-glucopyranose, oligomeric, decyl octyl glyco ALSO CALLED (3R,45,55,6R)-2-(DECYLOXY)-6-(HYDROXYMETHYL)OXANE View all synonyms (21)	DSIDES E-3,4,5-TRIOL, (3R,4	IS,5S,6R)-2-(Decyloxy)-6-(hydroxy				Share Profile
Hazards Properties Functional Uses Resources						
All Hazards View 🔻				Show PubMed Results	Request Assessment	Add to Comparison -
Group I Human		Group II and II* Human	Ecotox	Fate Ph	nysical Mult	Non-GSLT
GS Score C M R	DE	AISISIN N SNS	SNR IFS IFE AA CA	ATE P E RX	F Mult PBI	GW O Other
All Hazards LT-UNK			- pc H		- U -	R
Hazard Lists						🛓 Download Lists
HAZ/	ARD GS	LIST NAME	HAZARD DESCRIPTION			OTHER
Skin Trritation/Corrosivity	NoGS	EU - Manufacturer REACH bazard	H315 - Causes skin irr	itation (unverified)		LIGIO
		submissions				
Eye Irritation/Corrosivity	LT- UNK	GHS - New Zealand	6.4A - Irritating to t	the eye (Cat. 2A)		+2
Dq	NoGS	EU - Manufacturer REACH hazard submissions	H318 - Causes serious	eye damage (unverified))	
PC	NoGS	EU - Manufacturer REACH hazard	H319 - Causes serious	eye irritation (unverif	fied)	

			submissions	
Human and/or Aquatic toxicity and/or Persistence and/or Bioaccumulation	U	LT- UNK	German FEA - Substances Hazardous to Waters	Class 1 - Low Hazard to Waters
T & P and/or B [(Chronic Aquatic Toxicity and Persistence) or (Acute Aquatic Toxicity and Persistence and/or Bioaccumulation)]	U	LT- UNK	GHS - New Zealand	9.1D (algal) - Slightly harmful in the aquatic environment or are otherwise designed for biocidal action
	U	LT- UNK	GHS - New Zealand	9.1D (crustacean) - Slightly harmful in the aquatic environment or are otherwise designed for biocidal action

Restricted Substance Lists (1)

• EU - PACT-RMOA Substances: Substances selected for RMOA or hazard assessment

Positive Lists (3)

- Cosmetic Ingredient Review (CIR): Safe with Qualifications
- + Inventory of Existing Cosmetic Ingredients in China (IECIC 2015): Cosmetic Ingredients
- US EPA DfE SCIL: Green Circle Verified Low Concern

Discussions

No discussions have been posted yet.

Ask a question about this chemical in the forums >

APPENDIX D: U.S. EPA Bioactivity (EDSP21) Summary for D-Glucose (CAS #50-99-7)



<u>APPENDIX E: U.S. EPA Bioactivity (ToxCast Models) Summary for D-Glucose</u> (CAS #50-99-7)

	D-Glucose 50-99-7 DTXSID7022910 Searched by DSSTox Substance Id.				
DETAILS		ToxCa	st: Models		
EXECUTIVE SUMMARY		ToxCast M	odel Predictions		
PROPERTIES	🕹 Download ToxCast Model Predictions ▼				
ENV. FATE/TRANSPORT					
HAZARD	Model	Receptor	Agonist	Antagonist	Binding
HAZARD	ToxCast Pathway Model (AUC)	Androgen	-	-	-
SAFETY	ToxCast Pathway Model (AUC)	Estrogen			
ADME	COMPARA (Consensus)	Androgen	Inactive	Inactive	Inactive
EXPOSURE	CERAPP Potency Level (From Literature)	Estrogen			
, Darosone	CERAPP Potency Level (Consensus)	Estrogen	Inactive (Inactive)	Inactive (Inactive)	Inactive (Inactive)
▼ BIOACTIVITY					
TOXCAST: SUMMARY					

APPENDIX F: U.S. EPA Bioactivity (EDSP21) Summary for Octanoic Acid (CAS #124-07-2)









PUBCHEM

APPENDIX G: U.S. EPA Bioactivity (ToxCast Models) Summary for Octanoic Acid (CAS #124-07-2)

EPA United States Environmental Pro Agency	tection Home Advanced Search Batch Search Lists 🕶 Predictions Downloads		Сору 🔻	Share Submit Comment	Search all data
	Octanoic acid 124-07-2 DTXSID3021645 Searched by CAS-RN.				
DETAILS		ToxCa	st: Models		
EXECUTIVE SUMMARY		ToxCast M	odel Predictions		
PROPERTIES	★ Download ToxCast Model Predictions ▼				
ENV. FATE/TRANSPORT					
	Model	Receptor	Agonist	Antagonist	Binding
HAZARD	ToxCast Pathway Model (AUC)	Androgen	0.00	0.00	
SAFETY	ToxCast Pathway Model (AUC)	Estrogen	4.57e-3	1.42e-2	
ADME	COMPARA (Consensus)	Androgen	Inactive	Inactive	Inactive
EXPOSURE	CERAPP Potency Level (From Literature)	Estrogen	Inactive (Inactive)	Inactive (Inactive)	Inactive (Inactive)
,	CERAPP Potency Level (Consensus)	Estrogen	Inactive (Inactive)	Inactive (Inactive)	Inactive (Inactive)
 BIOACTIVITY 					
TOXCAST: SUMMARY					
EDSP21					
TOXCAST/TOX21					

<u>APPENDIX H: OECD Toolbox Profile for D-Glucopyranose, Oligomers, Decyl Octyl</u> <u>Glycosides (CAS #68515-73-1)</u>

QSAR Toolbox 4.4.1 [Document 1]			
QSAR TOOLBOX	T T T nput Profiling > Data	Category definition	► Report
Profiling Custom profile Image: Custom profile Image: Custom profile Image: C			
Documents	Filter endpoint tree 🍸	1 [target]	
 Document 1 # [C: 1;Md: 0;P: 0] CAS: 68515731 Profiling methods Options 4 3 Selected 	Structure	нзс~~~~ оч но с он но с он но с он	
f Select All Unselect All Invert	SMILES	CCCCCCCCCCCCC1OC(COC2OC(CO)C(O)C(O)C	
Carcinogenicity (genotox and nongenot	🕀 Parameters		
DART scheme	Physical Chemical Properties		
	Environmental Fate and Transport		
	Ecotoxicological Information		
Metabolism/Transformations	🛨 Human Health Hazards	•	
Options OSelected			
f Select All Unselect All Invert		No Lot formed	
Observed Mammalian metabolism	Carcinogenicity (genotox and nongen	Not classified	
Observed Microbial metabolism		No alert found	
Chserved Rat In vivo metabolism	Respiratory sensitisation	No alert found	
	<		
1			

APPENDIX I: Known Structural Alerts for Reactivity

Explosivity – Abbreviated List

 Not classified if 	no chemical groups associated with
explosivity, e.g.	ne enemiear groupe accordice with
Structural feature	Chemical classes
C–C unsaturation (not aromatic rings)	Acetylenes, acetylides, 1,2-dienes
C-metal, N-metal	Grignard reagents, organolithium compounds
Contiguous oxygen	Peroxides, ozonides
N–O bonds	Hydroxylamines, nitrates, nitro compounds, nitroso compounds, N-oxides, 1,2-oxazoles
N-halogen	Chloramines, fluoramines
O-halogen	Chlorates, perchlorates, iodosyl compounds
Contiguous nitrogen atoms	Azides, azo compounds, diazo compounds, hydrazines
Strained ring structure	Cyclopropanes, aziridines, oxiranes, cubanes

Explosivity – Full List

Chemical group	Chemical Class
-C=C-	Acetylenic Compounds
-C=C-Metal	Metal Acetylides
-C=C-Halogen	Haloacetylene Derivatives
CN2	Diazo Compounds
-N=O -NO2	Nitroso and Nitro Compounds,
R-O-N=O R-O-NO ₂	Acyl or Alkyl Nitrites and Nitrates
≥c-c≤	1,2-Epoxides
C=N-O-Metal	Metal Fulminates or aci-Nitro Salts
N-Metal	N-Metal Derivatives (especially heavy metals)
N-N=O N-NO2	N-Nitroso and N-Nitro Compounds
N−N−NO ₂	N-Azolium Nitroimidates
	Azo Compounds
Ar-N=N-O-Ar	Arene Diazoates
(ArN=N)2O, (ArN=N)2S	Bis-Arenediazo Oxides and Sulfides
RN=N-NR'R''	Triazines
$\begin{array}{c} N \stackrel{N}{=} N \\ I \\ R' $	High-nitrogen Compounds: e.g. Triazoles, Tetrazoles

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

Chemical group	Chemical Class
[1] ROOR',	Peroxy Compounds:
-050	 Alkyl hydroperoxides (R'=H), Peroxides (R'=organic);
[2] `OOR'	[2] Peroxo acids (R'=H), Peroxyesters (R'=organic)
[1] ROOMetal,	Metal peroxides, Peroxoacids salts
$-c^{\circ O}_{OO^{\bullet} Metal^{+}}$	
-N ₃	Azides e.g. PbN ₆₀ CH ₃ N ₃
0C-N ₂	Arenediazonium oxides i.e. inner diazonium salts in which the counter ion is an oxide
Ar-N=N-S-	Diazonium sulfides and derivatives, Arenediazo Arvl Sulfides
Ar-N=N-S-Ar	
XO _n	Halogen Oxide: e.g. percholrates, bromates, etc
NX3 e.g. NC13, RNC12	N-Halogen Compounds

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

Self-Reactive Substances

ई Screer	ning procedures
 Not in CLP, but Appendix 6 	UN Manual of Tests and Criteria
 No explosive gr 	oups (see 2.1) plus
Structural feature	Chemical classes
Mutually manuf	A 1 10 10 10 10 10 10 10 10 10 10 10 10 1
Mutually reactive groups	Aminonitriles, haloanilines, organic salts of oxidising agents
S=O	Aminonitriles, haloanilines, organic salts of oxidising agents Sulphonyl halides, sulphonyl cyanides, sulphonyl hydrazides
S=O P–O	Aminonitriles, haloanilines, organic salts of oxidising agents Sulphonyl halides, sulphonyl cyanides, sulphonyl hydrazides Phosphites
S=O P–O Strained rings	Aminonitriles, haloanilines, organic salts of oxidising agents Sulphonyl halides, sulphonyl cyanides, sulphonyl hydrazides Phosphites Epoxides, aziridines

Licensed GreenScreen[®] Profilers

D-Glucopyranose, Oligomers, Decyl Octyl Glycosides GreenScreen[®] Evaluation Prepared by:



Mouna Zachary, PhD Toxicologist ToxServices LLC

D-Glucopyranose, Oligomers, Decyl Octyl Glycosides GreenScreen[®] Evaluation QC'd by:



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