Australian Government
Department of Health and Aged Care
Australian Industrial Chemicals Introduction Scheme

.alpha.-D-Glucan, (1→2),(1→6)-, 2-hydroxy-3-(trimethylammonio)propyl ether, chloride

Assessment statement (CA09824)

11 June 2024

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AICIS assessment (CA09824)

Chemical in this assessment

Name	CAS registry number
.alpha.-D-Glucan, (1→2),(1→6)-, 2-hydroxy-3-(trimethylammonio)propyl ether, chloride	2412833-99-7

Reason for the assessment

An application for an assessment certificate under section 31 of the *Industrial Chemicals Act 2019* (the Act).

Certificate Application type

AICIS received the application in a Very Low to Low Risk type.

Defined scope of assessment

The chemical has been assessed as:

- imported into Australia at up to 15 tonnes per annum;
- imported as a component of formulations containing at up to 33.5% concentration for local reformulation into finished cosmetic products containing the assessed polymer at up to 2% concentration for consumer and professional use; and
- imported as a component of finished laundry products at up to 0.68% concentration for consumer use only.

Summary of assessment

Summary of introduction, use and end use

The assessed polymer will not be manufactured in Australia. It will be imported into Australia in formulations containing the assessed polymer at up to 33.5% concentration for further local reformulation into finished end use cosmetic products at up to 2% concentration. The assessed polymer will also be imported as a component of finished laundry products at up to 0.68% concentration for consumer use only.

Reformulation activity will not take place at the applicant's Australian facilities. The drums containing the assessed polymer at up to 33.5% concentration will be sold to the downstream users for blending with other ingredients to produce finished end use cosmetic products.

Finished cosmetic products containing the assessed polymer will be widely used by both consumers and professionals (such as beauticians and hairdressers). Depending on the nature of the product, application may be by hand, through the use of an applicator or spray. The proposed cosmetic end use products include soaps, hair care products (liquid and spray), nail care products, and skin care products (non-soap). The typical function of the assessed polymer in these cosmetic products is stated to be that of softener and conditioner.

Finished laundry products containing the assessed polymer will be widely used by consumers.

Human health

Summary of health hazards

The submitted toxicological data on the assessed polymer (see **Supporting information**) indicate that the assessed polymer is:

- of low acute oral toxicity
- not irritating to skin and eyes
- not expected to be a skin sensitiser
- not expected to be genotoxic.

No acute dermal, acute inhalation toxicity or repeated dose toxicity data were provided for the assessed polymer. However, as limited absorption is expected across biological membranes (see **Supporting information**), systemic effects from repeated exposure are expected to be limited.

Hazard classifications relevant for worker health and safety

Based on the data provided by the applicant, the assessed polymer does not satisfy the criteria for classification according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE 2017) for hazard classes relevant for worker health and safety as adopted for industrial chemicals in Australia.

Summary of health risk

Public

When introduced and used in the proposed manner, there will be widespread and repeated exposure of the public to the assessed polymer at up to 2% concentration through the use of a wide range of cosmetic and laundry products. The principal route of exposure will be dermal, while ocular and inhalation exposures are also possible.

This assessment does not identify any risks to public health that would require specific risk management measures.

Workers

The applicant stated that reformulation activity will not take place at the applicant's Australian facilities. Workers may experience exposure to the assessed polymer at up to 33.5% concentration (as liquid) during reformulation processes such as weighing and transfer, blending, quality control analysis, filling and repackaging, and cleaning and maintenance of equipment, particularly where manual or open processes are used. The applicant expects that reformulation will be automated and that engineering controls such as local ventilations and enclosed processes will be in place to minimise exposure. The applicant expects that personal protective equipment (PPE) such as safety goggles, chemically impervious gloves and coveralls will be worn by reformulation workers. Therefore, considering the use of engineering controls and PPE, minimal exposure is expected to workers during reformulation.

Exposure to the assessed polymer in end-use products (at up to 2% concentration) may occur in professions where the services provided involve the application of cosmetic products to

clients (e.g., hairdressers and workers in beauty salons). These products, depending on their nature, could be applied in several ways, such as by hand, using an applicator or sprayed. The principal route of exposure will be dermal although inhalation and ocular exposures are also possible from spray products.

Professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using the end use products containing the assessed polymer at up to 2% concentration.

As limited absorption is expected across biological membranes (see **Supporting information**), this assessment does not identify any risks to the workers that would require specific risk management measures.

Environment

Summary of environmental hazard characteristics

According to domestic environmental hazard thresholds and based on the available data, the assessed polymer is:

- Not Persistent (not P)
- Not Bioaccumulative (not B)
- Not Toxic (not T)

Environmental hazard classification

Based on the ecotoxicological information available for the assessed polymer, it is not expected to be harmful to aquatic life. Therefore, the assessed polymer is not formally classified under the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE 2017) for acute and chronic aquatic toxicities.

Summary of environmental risk

The assessed polymer will be introduced as a softening and conditioning ingredient for use in a variety of cosmetic products such as soap, hair care and nail care products. Use of the assessed polymer in these products is expected to result in the release of the assessed polymer “down the drain” and into the sewers. Consequently, the assessed polymer will be treated at sewage treatment plants (STPs) before release to surface waters.

The assessed polymer does not meet any of the PBT criteria and is hence unlikely to have unpredictable long-term effects. As the assessed polymer is not expected to be harmful to aquatic organisms, the introduction of the assessed polymer, in line with the terms outlined in this assessment statement, is not expected to pose a significant risk to the environment. As such, the risk from the assessed polymer can be managed.

Means for managing risk

Workers

Information relating to safe introduction and use

As limited absorption is expected across biological membranes (see **Supporting information**), this assessment does not identify any risks to workers that would require specific risk management measures.

Conclusions

The Executive Director is satisfied that the identified risks to human health and the environment from the introduction and use of the industrial chemical can be managed.

Note:

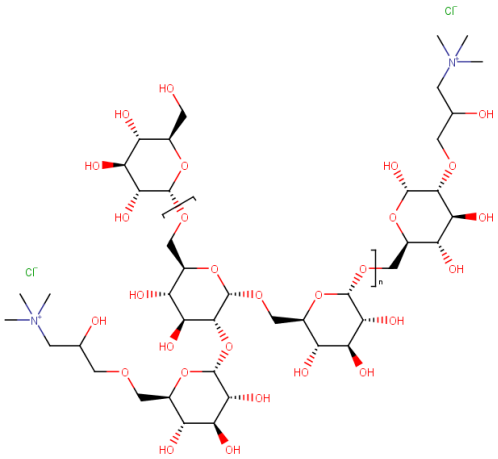
1. Obligations to report additional information about hazards under s 100 of the *Industrial Chemicals Act 2019* apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Chemical identity

Chemical name	.alpha.-D-Glucan, (1→2),(1→6)-, 2-hydroxy-3-(trimethylammonio)propyl ether, chloride
CAS No.	2412833-99-7
Molecular formula	$C_6H_{16}NO_2$.xCl.xUnspecified
Molecular weight	NAMW > 100,000 g/mol

Representative structure



Chemical description:

The assessed polymer has a purity of greater than or equal to 99.9%.

Relevant physical and chemical properties

Physical form	Off white powder
Density	1,500 kg/m^3 *
Water solubility	10 g/L at 24 °C and pH 7
Ionisable in the environment?	Yes
p*K*a	12 (based on read across from common sugars)
log K_{ow}	-4.5 at 30 °C and -3.85 at 25 °C

* Derived from analogue data

Health hazard information

Toxicokinetics

Absorption of the assessed polymer across biological membranes is expected to be limited, based on the high molecular weight of the assessed polymer. Limited absorption is further supported by data from a dermal absorption study in Fischer 344 rats on an analogue polymer. A maximum absorption of 1.75% was observed in the rats after treatment with the analogue polymer at 5% concentration.

Acute toxicity

Oral

In an acute oral toxicity study (OECD TG 423), female Wistar rats (n = 3/group) were administered the assessed polymer as a single dose of 300 and 2,000 mg/kg bw via oral gavage. The animals were observed for 14 days after administration. All animals survived until the end of the 14-day study period and no sign of clinical toxicity was noted. All animals showed the expected body weight gains over the study period. No treatment related gross necropsy findings were observed. The acute oral median lethal dose (LD50) of the assessed polymer was determined to be greater than 2,000 mg/kg bw.

Corrosion/Irritation

Skin irritation

In an in vitro skin irritation test using the EpiDerm™ reconstructed human epidermis tissue model (EpiSkin kit) (OECD TG 439), the assessed polymer was tested by single topical applications of 10 mg (neat) test substance or 10 µL solution at 66% concentration of the test substance. The relative mean viability of the test substance-treated tissues, as compared to the negative control tissues, was 103.7% for the neat test substance and 79.5% for the test substance at 66% concentration after the 15-minute exposure period. These relative mean tissue viabilities are above the threshold for irritancy of ≤ 50% after the 15 ± 0.5 minutes treatment period (followed by a 42-hour post-exposure incubation period). Under the

conditions of the study and according to the test guideline, the assessed polymer is not considered to be irritating to the skin.

Eye irritation

The assessed polymer was tested for eye irritation potential by a single topical application of 50 mg undiluted test substance or 50 µL solution of the test substance at 33% and 66% concentration to a reconstructed Human Cornea-like Epithelium (RhCe) (EpiOcular™ model) (OECD TG 492). The relative mean tissue viability obtained after 6 hours exposure to the undiluted test substance was 66.9%. The relative mean tissue viability obtained after 32 minutes exposure to the test substance at 33% and 66% concentration was 84.3% and 88.2%, respectively. All mean tissue viabilities were greater than 60.0% relative to negative control-treated tissue viability. Therefore, under the conditions of the study and according to the test guideline, the assessed polymer is not considered to be irritating to eyes.

Sensitisation

Skin sensitisation

One *in chemico* and two in vitro cell based assays were conducted to evaluate the skin sensitisation potential of the assessed polymer at 28.7% concentration. These tests are part of the Integrated Approach to Testing and Assessment (IATA) which addresses specific key events of the Adverse Outcome Pathway (AOP) leading to development of skin sensitisation (OECD, 2016).

The direct peptide reactivity assay (DPRA) is an *in chemico* method and aims to address the first key event (KE) (molecular initiation) of the AOP by measuring the interaction of the assessed polymer with cysteine and lysine, small synthetic peptides representing the nucleophilic centres in skin proteins (OECD TG 442C). The ARE-Nrf2 luciferase assay aims to address the second key event (keratinocyte activation) of the AOP by measuring the expression of a reporter luciferase gene under the control of a promoter from the antioxidant response element (ARE), a responding gene known to be upregulated by contact sensitisers (OECD TG442D). In the third key event assay, the Human Cell Line Activation test (h-CLAT) assay, the skin sensitisation potential of the test substance is evaluated by measuring the changes in the expression of cell surface markers (CD54 and CD86) associated with the process of dendritic cell activation in the human leukemia cell line (THP-1) following exposure to the test substance (OECD TG 442E). The results of these assays are considered using the applicable defined approach (DA) in the Defined Approaches on Skin Sensitisation (DASS) Guideline (OECD GL 497, June 2021) for Classification and Labelling purposes. The assessed polymer at 28.7% concentration was positive in the DPRA and negative in the ARE-Nrf2 luciferase assay and h-CLAT assays. Based on these results and using the DA ‘two out of 3’ in the DASS Guideline, the assessed polymer is not a skin sensitiser at the tested concentration of 28.7%.

The skin sensitisation potential of the assessed polymer was further tested in a human repeat insult patch test (HRIPT) study in 240 subjects The study was conducted as per Clinical Study Protocol CL 1.0 2022 and following applicable ICH GCP standards to ensure reliability of data, subject safety, and confidentiality. A total of 231 human subjects (female and/or male, 19–70 years old), out of 240 enrolled, satisfactorily completed the test procedure. A total of nine subjects (9/240) discontinued due to reasons unrelated to the test material. The assessed polymer, as neat in a powder form, was mixed with distilled water before patching semi-occlusively to the same location on the back of each subject three times per week for a total of nine applications during the induction phase, with 24-hour rest periods. After approximately 10 to 21 days after the final Induction Phase, subjects were rechallenged at a virgin site on the

back for 24 hours. The proportion of volunteers that presented an allergic reaction was 0%. Therefore, under the conditions of the HRIPT study, the assessed polymer at 100% concentration did not demonstrate a potential for eliciting dermal irritation or inducing sensitisation.

Genotoxicity

The assessed polymer was found to be non-mutagenic in a bacterial reverse mutation assay using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and *Escherichia coli* strain WP2uvrA (pKM101), with or without metabolic activation (S9-mix) (OECD TG 471). No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains at any tested concentration (50, 158, 500, 1,581, 5,000 µg/plate), with or without metabolic activation (S9-mix).

The assessed polymer was also found to be non-mutagenic in an in vitro Mammalian Cell Micronucleus test using human lymphocytes, with or without metabolic activation (S9) (OECD TG 487). Three independent experiments were performed. Experiments 1 and 2 included a 3-hour exposure with or without metabolic activation, and experiment 3 included a 24-hour exposure without metabolic activation. Blood cultures were exposed to the assessed polymer in duplicate at concentrations of 312.5, 1,250 and 5,000 µg/mL in all three experiments. No evidence of statistically significant induction of micronuclei was reported with or without metabolic activation in any of the tested concentrations.

Overall, the assessed polymer is not considered to be genotoxic.

Environmental exposure

The assessed polymer will be imported into Australia either as a component in finished end-use products or as a component of liquid formulations for reformulation into end-use products. Reformulation will occur through closed processes. Significant releases of the assessed polymer to the environment are not expected during reformulation, transport or storage. Release of the products containing the assessed polymer to the environment due to accidental spills is expected to be absorbed on suitable materials, and disposed of in accordance with relevant Local, State, Territory and Federal regulations. Any unused product containing the assessed polymer is expected to be disposed of in accordance with relevant Local, State, Territory and Federal regulations.

The assessed polymer is a softening and conditioning ingredient to be included in cosmetic products such as soap, hair care and nail care products. Use of these products is expected to result in the release of the assessed polymer “down the drain” and into the sewers. Consequently, the assessed polymer will be treated at sewage treatment plants (STPs) before release to surface waters.

Environmental fate

Partitioning

As the assessed polymer is a potential cationic polymer, it is expected to have low mobility in soil and sediment due to ion exchange mechanisms (US EPA, 2013).

The assessed polymer is readily soluble in water (water solubility = 10 g/L). If the assessed polymer is released to surface waters, a proportion of the assessed polymer is expected to remain in the water compartment with the remaining expected to partition to sediment, based on its ready solubility in water, high molecular weight and its potential cationicity.

As the assessed polymer has a high molecular weight, its vapor pressure and volatility are expected to be negligible (US EPA, 2013).

Degradation

Based on measured biodegradation in water, the assessed polymer is considered not persistent.

In a ready biodegradation screening test conducted in water (OECD TG 301B), the assessed polymer showed 92.9% degradation after 29 days, and the 10-day-window criterion was satisfied. Therefore, the assessed polymer is readily biodegradable.

In a hydrolysis test (OECD TG 111), the assessed polymer was hydrolytically stable with a half-life > 1 year.

Bioaccumulation

Based on its high molecular weight, the assessed polymer is considered not bioaccumulative.

No bioaccumulation information was provided for the assessed polymer. The assessed polymer has a high molecular weight (NAMW = 114,000 Da, 0.037% < 1,000 Da and 0.002% < 500 Da), which is usually of low concern for bioaccumulation (US EPA, 2013). In addition, the measured log K_{ow} of the assessed polymer is -3.85 and -4.5 which is below the domestic bioaccumulation threshold of log K_{ow} = 4.2 (EPHC, 2009). Therefore, the assessed polymer is considered not bioaccumulative.

Predicted environmental concentration (PEC)

A predicted environmental concentration (PEC) for Australian waters was calculated assuming 100% of the introduction volume is released into sewage treatment plants (STPs) over 365 days per annum. This calculated value is conservative as not all uses of the assessed polymer are expected to result in 100% release to STPs. As the assessed polymer is a potential cationic polymer with NAMW far above 1,000 Da, its removal through STP process is expected to be 90% (US EPA, 2013). Therefore 10% of the total introduction volume is estimated to be released to the aquatic environment. The calculation of the PEC is detailed in the table below:

Total Annual Import Volume	15,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	15,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release	41.1	kg/day
Water use	200	L/person/day
Population of Australia	25.423	Million
Removal within STP	90%	Mitigation
Daily effluent production	5,085	ML/day
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River	0.89	µg/L
PEC - Ocean	0.09	µg/L

Environmental effects

Effects on aquatic Life

Acute toxicity

The following measured median lethal concentration (LC50) and median effective concentration (EC50) values for model organisms were provided for the assessed polymer:

Taxon	Endpoint	Method
Fish	96 h LC50 > 400 mg/L	*Pimephales promelas* (Fathead minnow) Mortality OECD TG 203 Static conditions Nominal concentration
Invertebrate	48 h EC50 > 400 mg/L	*Daphnia magna* (Water flea) Immobility OECD TG 202 Static conditions Nominal concentration
Algae	96 h ErC50 > 120 mg/L	*Raphidocelis subcapitata* (Green algae) Growth rate inhibition OECD TG 201 Static conditions Nominal concentration

Chronic toxicity

The following measured no-observed-effect concentration (NOEC) value for model organism was provided for the assessed polymer:

Taxon	Endpoint	Method
Algae	96 h NOEC = 1.2 mg/L	*Raphidocelis subcapitata* (Green algae) Growth rate inhibition OECD TG 201 Static conditions Nominal concentration

Predicted no-effect concentration (PNEC)

A predicted no-effect concentration (PNEC) was not calculated as the assessed polymer is not expected to be harmful to aquatic organisms.

Categorisation of environmental hazard

The categorisation of the environmental hazards of the assessed polymer according to domestic environmental hazard thresholds is presented below:

Persistence

Not Persistent (Not P). Based on a measured degradation study in water, the assessed polymer is categorised as Not Persistent.

Bioaccumulation

Not Bioaccumulative (Not B). Based on its high molecular weight, the assessed polymer is categorised as Not Bioaccumulative.

Toxicity

Not Toxic (Not T). Based on available ecotoxicity values above 1 mg/L, the assessed polymer is categorised as Not Toxic.

Environmental risk characterisation

The assessed polymer is not PBT and is hence unlikely to have unpredictable long-term effects (EPHC, 2009). As the assessed polymer is not expected to be harmful to aquatic organisms, the introduction of the assessed polymer, in line with the terms outlined in this assessment statement, is not expected to pose a significant risk to the environment. As such, the risk from the assessed polymer can be managed, based on the low environmental hazard characteristics.

References

EPHC (2009) Environment Protection and Heritage Council, Environmental Risk Assessment Guidance Manual for industrial chemicals, Prepared by: Chris Lee-Steere Australian Environment Agency Pty Ltd, February 2009. ISBN 978-1-921173-41-7

UNECE (United Nations Economic Commission for Europe) (2017). Globally Harmonized System of Classification and Labelling of Chemicals (GHS), Seventh Revised Edition. UNECE.

US EPA (2013) Interpretive Assistance Document for Assessment of Polymers – Sustainable Futures Summary Assessment, US Environmental Protection Agency, https://www.epa.gov/sites/production/files/2015-05/documents/06-iad_polymers_june2013.pdf.