Australian Government
Department of Health
Australian Industrial Chemicals Introduction Scheme

1-Propanamine, 3,3'-[oxybis(2,1-ethanediyloxy)]bis-, (2Z)-2-butenedioate (1:2) (Bis-aminopropyl diglycol dimaleate)

Evaluation statement

28 February 2022

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AICIS evaluation statement

Subject of the evaluation

1-Propanamine, 3,3'-[oxybis(2,1-ethanediyloxy)]bis-, (2*Z*)-2-butenedioate (1:2) (Bis-aminopropyl diglycol dimaleate)

Chemical in this evaluation

Name	CAS registry number
1-Propanamine, 3,3'-[oxybis(2,1-ethanediyloxy)]bis-, (2*Z*)-2-butenedioate (1:2)	1629579-82-3

Reason for the evaluation

To evaluate information submitted by industry to meet their obligation according to the terms of the assessment certificate.

The Executive Director decided to initiate the evaluation in order to assess the risks to human health from exposure to the chemical following notification from one of the assessment certificate holders on their proposed use of the chemical at concentrations higher than 0.1% in haircare products.

Defined scope of the evaluation

The chemical, 1-propanamine, 3,3'-[oxybis(2,1-ethanediyloxy)]bis-, (2*Z*)-2-butenedioate (1:2) (CAS No. 1629579-82-3), was assessed in June 2020 as a new industrial chemical in the standard notification category (STD/1684) under *Section 23* of the *Industrial Chemicals Notification and Assessment (ICNA) Act 1989* (NICNAS 2020).

Under *Section 101* of the *Industrial Chemicals (IC) Act 2019,* the introducer has provided new information indicating that the chemical is to be imported as a component of finished haircare products at up to 20% concentration. The chemical is also to be used as a component of haircare products by the public at a concentration of up to 13.75%. In addition, human health hazard information in the form of human repeat insult patch test (HRIPT) studies with the chemical at up to 19% concentration was submitted.

As the concentration of the chemical previously assessed was <0.1% concentration in haircare products, the increased concentration of the chemical in haircare products was considered a significant change in the circumstances from the originally assessed introduction (NICNAS 2020).

This evaluation provides information on the identified risk to public and workers associated with the significant change of introduction for the chemical and whether the human health risks from any change in introduction can be managed within existing risk management frameworks.

This evaluation report should be read in conjunction with the assessment report STD/1684 (NICNAS 2020).

Summary of evaluation

Summary of introduction, use and end use

The chemical is not manufactured in Australia, and up to 50 tonnes of the chemical is imported into Australia as a component of finished haircare products at 3%, 13.75%, and 20% concentration. While fully finished haircare products at 20% concentration are available for professional use only, the other 2 fully finished haircare products (3% and 13.75% concentration) are available for public use. Professionals (such as beauticians and hairdressers) will further dilute the haircare product at 20% concentration with water, resulting in a final chemical concentration of 2.9% for application. End use products containing the chemical at various concentration will be widely used by consumers and professionals such as hairdressers and workers in salons.

Human health

Summary of health hazards

In the previous assessment under NICNAS, based on the results of the adverse outcome pathway (AOP) studies, the chemical was classified as a skin sensitiser (H317: May cause an allergic skin reaction) (NICNAS 2020). The introducer has submitted 7 HRIPT studies on the chemical at concentrations between 1.2% and 19% in demineralised water using a standard methodology. An allergic reaction was not noted in any of the seven studies submitted, including the study conducted with the highest concentration (19%) of the chemical (see **Supporting Information**). The results concluded that the chemical is non-sensitising under the conditions of the test at up to the highest tested concentration of 19%. The negative human data assessed in this evaluation does not negate the classification for skin sensitisation recommended in the previous assessment (STD/1684).

The toxicological investigations conducted on the chemical are discussed in full detail in the assessment report STD/1684 (NICNAS 2020). The available data indicates that the chemical:

- is likely to have limited dermal absorption, based on low partition coefficient (log Pow = -2.8 to -2.4 at 20 °C)
- is likely to be of low acute oral and dermal toxicity
- is non-irritating to the skin and eyes
- may have potential for systemic toxicity at high concentrations following repeated oral exposure
- is not considered to be genotoxic.

Summary of health risk

Public

Information submitted as a result of a specific information obligation revealed that the public may experience repeated exposure to the chemical at up to 13.75% concentration with the use of haircare products. The principal route of exposure will be dermal, while ocular and

inhalation exposure are also possible, particularly if products are applied by spray. The frequency and extent of public exposure is expected to be lower than that for professional workers.

The new HRIPT data assessing the use of the chemical at up to 19% concentration indicated that skin sensitisation effects are not expected from the use of haircare products containing the chemical at up to 13.75%.

The repeated dose toxicity effects of the chemical have not been determined. Analogue chemical data in the original assessment indicated that the chemical may have potential for systemic toxicity. However, given the limited potential for dermal absorption based on physico-chemical properties and the lower daily exposure of haircare products compared to other personal care products, systemic toxicity effects are not expected under the proposed use.

Therefore, there are no identifiable risks to the public health that require further management. However, if new information on the chemical becomes available indicating skin sensitisation and systemic toxicity, further risk management may be required.

Workers

Workers involved in professions which involve application of haircare products containing the chemical to clients (e.g. hairdressers and beauty salon workers), may be exposed to the chemical at up to 20% concentration. The principal route of exposure is dermal, while accidental ocular and inhalation exposure are also possible, particularly if haircare products are applied by spray. Beautician and hairdresser professionals may use some personal protective equipment (PPE) to minimise repeated exposure, and good hygiene practices are expected to be in place. Although data on the sensitisation potential at 20% are not available, results from HRIPT studies indicate low potential for sensitisation at up to 19%. However, with repeated exposure expected, sensitisation effects cannot be ruled out. Control measures to minimise dermal exposure are needed to manage the risk to workers (refer to **Proposed means for managing risk** section).

Proposed means for managing risk

Workers

Information relating to safe introduction and use

The information in this statement, should be used by a person conducting a business or undertaking (PCBU) at a workplace (such as an employer), to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.

Control measures that could be implemented to manage the risk arising from dermal exposure to the chemical include but are not limited to:

- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using personal protective equipment (PPE) that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

These control measures may need to be supplemented with:

- conducting health monitoring for any worker who is at significant risk of exposure to the chemical, if valid techniques are available to monitor the effect on the worker's health.

Model codes of practice, available from the Safe Work Australia website, provide information on how to manage the risks of hazardous chemicals in the workplace, prepare an SDS and label containers of hazardous chemicals. Your Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

Conclusions

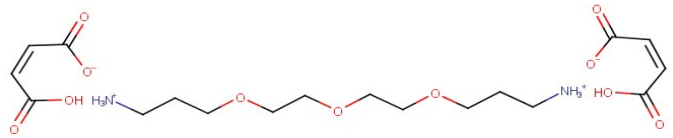
The conclusions of this evaluation are based on the information described in this statement.

Considering the proposed means of managing risks, the Executive Director is satisfied that, when the chemical is introduced and used in accordance with the terms of the assessment certificate (refer to **Supporting information**) the identified human health risks can be managed within existing risk management frameworks. This is provided that all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory and the proposed means of managing the risks identified during this evaluation are implemented.

Note: Obligations apply to report additional information about hazards under *Section 100* of the *IC Act 2019* and to provide any information specifically required by the terms of the assessment certificate under *Section 101*, of the *IC Act 2019*.

Supporting information

Chemical identity

Chemical Name	1-Propanamine, 3,3'-[oxybis(2,1-ethanediyloxy)]bis-, (2Z)-2-butenedioate (1:2)
CAS No	1629579-82-3
Synonyms	bis-aminopropyl diglycol dimaleate (INCI name; marketing name) 3-{2-[2-(3-azaniumylpropoxy)ethoxy]ethoxy}propan-1-aminium di[(2Z)-3-carboxyprop-2-enoate] (other name)
Structural formula	
Molecular formula	C10H24N2O3.2C4H4O4
Molecular weight (g/mol)	452.46
SMILES	O=C(O)C=CC(=O)O.O(CCOCCCN)CCOCCCN
CAS Number	1629579-82-3

Existing Australian regulatory controls

AICIS

The chemical is currently authorised to be introduced as an assessed introduction with the following terms of the assessment certificate:

Specific requirements to provide information to the Executive Director under Section 101 of the IC Act	Obligations to provide information apply. You must tell us within 28 days if: • the final use concentration of the notified chemical is ≥ 0.1% in haircare products • the notified chemical is to be used as a component of cosmetic products, other than for haircare • additional toxicological information becomes available on the notified chemical, in particular, studies on genotoxicity or skin sensitisation • the notified chemical has begun to be reformulated in Australia to be used in haircare products • the function or use of the chemical has changed, or is likely to change significantly • the amount of chemical being introduced has increased, or is likely to increase, significantly • in the case of a chemical not manufactured, or proposed to be manufactured, in Australia at the time of the assessment - it has begun to be manufactured in Australia • the method of manufacture of the chemical in Australia has changed, or is likely to change, in a way that may result in an increased risk of an adverse effect of the chemical on occupational health and safety, public health or the environment • additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

Note: Under *Section 11(2)(e) of Industrial Chemicals (Consequential Amendments and Transitional Provisions) Act 2019*, the notification obligations under *Subsections 64(1) and (2) of the old law (ICNA Act)* are taken to be specific requirements to provide information to the Executive Director.

Health hazard information

The new health hazard information provided is summarised below. For additional supporting health hazard information, refer to the STD/1684 public report (NICNAS 2020).

Skin sensitisation

The introducer has submitted 7 HRIPT studies on the chemical at concentrations between 1.2% and 19% in demineralised water using a standard methodology. No allergic reaction

was noted in any of the 7 studies submitted. The two studies conducted with the highest concentration (18%, 19%) of the chemical are presented below.

A HRIPT with challenge study was conducted as per the 'adaptation of the modified Draize human sensitisation test' (semi-occlusive test patch) and completed with 100 subjects (no withdrawal).

In a study, volunteers (100 female and/or male 18–64 years old) were treated with the chemical at 18% concentration in demineralised water on the lower or upper back under semi-occlusive patch for 48 hours. For the negative control patch, 0.2 ml of demineralised water was applied in a patch. Treatment sites were assessed before the first application of test material (baseline) and 30 minutes after each patch application. The treatment was repeated 9 times on the same site during the 3 consecutive week induction period.

After a rest period of 2 weeks, a patch was applied to the induction site as well as to a virgin site (previously unpatched skin site) for 48 hours (challenge). This site was evaluated just after patch removal, 30 minutes and 48 hours after removal. Skin reactions were scored throughout the test by the same experienced assessor who made the baseline assessment and under the same lighting source, following a pre-defined irritation and sensitisation scoring scales.

Throughout the study, the number of volunteers that presented an irritant reaction was 4 percent (4%). The number of volunteers that presented an allergic reaction was zero percent (0%).

The test substance was non-sensitising under the conditions of the test.

In another study, volunteers (100 female and/or male 18-64 years old) were treated with the chemical at 19% concentration in demineralised water on the lower or upper back under occlusive patch for 48 hours. For the negative control patch, 0.2 ml of demineralised water was applied in a patch. The conditions, treatment protocol and scoring were performed similar to the aforementioned study.

Throughout the study, the number of volunteers that presented an irritant reaction was one percent (1%). The number of volunteers that presented an allergic reaction was zero percent (0%).

The test substance was non-sensitising under the conditions of the test.

References

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2020) STD1684 Public Report *1-Propanamine, 3,3'-[oxybis(2,1-ethanediyloxy)]bis-, (2Z)-2-butenedioate (1:2)*, AICIS, accessed December 2021.