Poly(oxy-1,2-ethanediyl), .alpha.-[2-[(1-oxododecyl)amino]ethyl]-.omega.-hydroxy-: Human health tier II assessment

25 November 2016

CAS Number: 26635-75-6

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:www.nicnas.gov.au

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	lauric monoethanolamide, ethoxylate a-[2-[(1-oxododecyl)amino]ethyl]-?-hydroxypoly(oxy-1,2-ethanediyl) glycols, polyethylene, monoether with N-(2-hydroxyethyl)dodecanamide lauric acid monoethanolamide, ethoxylated polyethylene glycol mono(2-lauramidoethyl) ether
Structural Formula	
Molecular Formula	(C2H4O)nC14H29NO2
Molecular Weight (g/mol)	287.44
SMILES	CCCCCCCCCCCC(=O)NCCOCCO

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified.

International

The following international uses have been identified through:

Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; Handbook of Industrial Surfactants; and Product information.

The chemical has reported use as a non-ionic surfactant (Galleria).

The chemical has reported cosmetic use as an emulsifying and/or cleansing agent (CosIng). The chemical has reported use in personal care products, which may include shampoo, hand soap and bath products (such as bubble bath) (Product Bulletin Stepan; INCI). Recent data indicate that the chemical

is not likely to be widely available for cosmetic use with only a single documented use of the chemical, as PEG-3 lauramide, in cosmetic products in the United States (Personal Care Products Council 2011).

The chemical has reported domestic use including:

- in cleaning products (detergent); and
- in cleaning/washing agents (SPIN).

The chemical has reported domestic use in the SPIN database. Available North American databases do not give evidence for use of the chemical in consumer products, indicating the chemical is not likely to be widely available for domestic use.

The chemical has reported commercial use in industrial detergents.

Restrictions

Australian

The chemical may be synthesised through processes which may result in 1,4-dioxane as an impurity, although it is expected to be removed to low levels. This impurity (listed under dioxane) is controlled through listing in the Poisons Standard (Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) in Schedule 6, with schedule labelling required to apply above 100 ppm (Appendix G).

International

No known restrictions have been identified.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

No exposure standards were identified

Health Hazard Information

The chemical (CAS 26635-75-6) is a ethoxylated amide of dodecanoic (lauric) acid. The number of ethylene glycol (ethoxylate, EA) units can vary, with the number of ethoxylate units for cosmetic products ranging from 2-11 (PEG-2 lauramide, PEG-3 lauramide, PEG-5 lauramide, PEG-6 lauramide and PEG-11 lauramide (CosIng)).

Toxicity information was not available for the chemical. Information available for a related ethoxylated fatty acid amide (known as PEG-4 rapeseedamide) and another structurally related alkoylated amide with a similar fatty acid carbon chain length and predominantly low levels of alkoxylation (< 3) have been used as part of a 'read across' methodology to determine what toxic effects may reasonably be expected from the chemical. The read across toxicity data have also been supplemented with data for monoethanolamine (MEA) fatty acid amides such as lauramide MEA (which is a single ethoxylate unit) and cocamide MEA (as it has a similar chain length to lauramide), which are considered likely to represent worst case toxicity, other non-ionic surfactants (for local effects) and results of Quantitative Structure Activity Relationship (QSAR) modelling for the chemical (CAS 26635-75-6).

Toxicokinetics

No specific data were available for the chemical.

The chemical is a surfactant which may have low molecular weight (< 1000 Da) and is likely to be formulated in many cases with a high proportion of low molecular weight species < 500 Da; hence absorption across biological membranes is expected.

Amidases in the skin could potentially convert the chemical to lauric acid and ethoxylated MEA (CIR, 2015).

Acute Toxicity

Oral

No specific data are available for the chemical. Based on data for related chemicals, the chemical is expected to have low acute oral toxicity.

The related chemicals, PEG-4 rapeseedamide, another structurally related alkoxylated amide and lauramide MEA showed low acute oral toxicity in rats (median lethal dose (LD50) > 2000 mg/kg bw) (NICNAS, 2001; NICNAS, 2013; CIR, 2015).

Dermal

No specific data are available for the chemical. Based on data for related chemicals, the chemical is expected to have low acute dermal toxicity.

The related chemicals, PEG-4 rapeseedamide, another structurally related alkoxylated amide and cocamide MEA showed low acute dermal toxicity in rats (median lethal dose (LD50) > 2000 mg/kg bw) (NICNAS, 2001; NICNAS, 2013; CIR, 2015).

Inhalation

No specific data are available for the chemical.

Based on weight of evidence from two acute inhalation studies carried out to Organisation for Economic Co-operation and Development (OECD) Test Guidelines (TG), it was determined that the related chemical, PEG-4 rapeseedamide, does not meet the classification criteria for acute toxicity via inhalation. However, adverse effects as a result of acute inhalation exposure cannot be ruled out (NICNAS, 2013).

Corrosion / Irritation

Skin Irritation

No specific data are available for the chemical. Based on the available data for related chemicals and other non-ionic surfactants, the chemical is expected to be irritating to skin, although the extent of irritation cannot be determined. In the absence of data on the chemical, classification is considered warranted (refer **Recommendation** section).

The CAS number represents chemicals with a range of ethoxylate units. Typically, with other non-ionic surfactants, there was a general trend between the severity of irritation and the degree of ethoxylation (NICNAS). It is not certain that this trend exists for the chemical. An exemption to classification based on the number of ethoxylate units cannot be established based on the available data. However, should the irritation potential of a specific chemical under this CAS description be known, the classification can be revised based on this information.

The related chemical, PEG-4 rapeseedamide was reported as irritating to skin in a study performed in accordance with OECD TG 404. Erythema and oedema were reported. There was no corrosive effect on the skin; however, the skin irritation had not resolved within the study period in all animals (NICNAS, 2013). Another structurally similar alkoxylated amide with surfactant properties was persistently irritating to rabbit skin (NICNAS, 2001). For other non-ionic surfactants (ethoxylated alcohols) skin irritation was observed across a wide range of ethoxylation but chemicals with 1-3 ethoxylate units appeared to be more irritating than chemicals with more than four ethoxylate units (NICNAS). However, lauramide MEA was reported to be non-irritating in a Draize rabbit study (CIR, 2015).

Eye Irritation

No specific data are available for the chemical. Based on the available data for related chemicals and other non-ionic surfactants, the chemical is expected to be irritating to eyes, although the extent of irritation (and the potential for effects to be reversible) cannot be determined. In the absence of data on the chemical, classification is warranted (refer **Recommendation** section). The CAS number represents chemicals with a range of ethoxylate units. An exemption to classification based on the number of ethoxlate units cannot be established based on the available data. Should additional data become available to suggest that an alternate hazard classification for a specific chemical under this CAS description is warranted, this classification may be revised as appropriate.

The related chemical, PEG-4 rapeseedamide was reported to be slightly irritating to the eye in a study performed in accordance with OECD TG 405 (NICNAS, 2013). However, another structurally similar alkoxylated amide with surfactant properties was moderately irritating to rabbit eyes with corneal opacification observed in all animals (NICNAS, 2001). Lauramide MEA was reported to be highly irritating to the eye in a Draize rabbit study (CIR, 2015). Other non-ionic surfactants (ethoxylated alcohols between C9 to C19 with 2.5 to 15 ethoxy units) were reported to be moderately to severely irritating to the eyes of rabbits, when applied undiluted (HERA, 2009). Very low concentrations (0.1 %) were non-irritating, while concentrations between 1 and 10 % were slightly to moderately irritating. No clear relationship between the alcohol chain length or the number of ethoxylate groups and degree of irritation could be established (NICNAS).

Sensitisation

Skin Sensitisation

No specific data are available for the chemical. Based on the data for related chemicals, the chemical is not expected to have skin sensitisation potential.

Testing on the PEG-4 rapeseedamide, showed no skin sensitisation potential in guinea pigs and humans (NICNAS, 2013). Another structurally related alkoxylated amide and cocamide MEA were not skin sensitisers in guinea pig maximisation tests (NICNAS, 2001; CIR, 2015). The available information indicate that the chemical is unlikely to require hazard classification for skin sensitisation potential.

Repeated Dose Toxicity

Oral

No data are available for the chemical. Based on data for a related chemical, repeated oral exposure to the chemical is not expected to cause serious damage to health.

In a 28-day study in rats with PEG-4 rapeseedamide an irritant effect on the gastrointestinal tract (with associated inflammatory response) was observed. No significant systemic effects were reported. A no observed adverse effect level (NOAEL) was determined as 15 mg/kg bw/day in males and 150 mg/kg bw/day in females (NICNAS). However, these effects were not seen in a 90-day study, with a 28-day recovery period (OECD TG 408, n=5/sex/dose) with the same chemical. No significant treatment-related changes in mortality, food consumption, body weight development, macroscopic changes, clinical biochemistry, haematology and urinalysis parameters were noted. A NOAEL of 200 mg/kg bw/day was established for both sexes in the 90-day study (Test Facility, 2014).

A NOAEL of 1000 mg/kg bw/day was established in a 28-day study in rats with another structurally related alkoylated amide. Changes in urinary parameters were observed at lower doses but associated pathological changes were not observed (NICNAS, 2001).

Dermal

No data are available for the chemical.

Inhalation

No data are available for the chemical.

Genotoxicity

No data are available for the chemical. The chemical is expected to have low genotoxic potential based on results for related chemicals and QSAR modelling predictions.

The related chemical, PEG-4 rapeseedamide was negative for genotoxic potential in an in vitro bacterial reverse mutation assay, an in vitro chromosome aberration test in mammalian cells (human lymphocytes) and an in vivo mouse micronucleus assay (NICNAS, 2013). Another stucturally related alkoxylated amide was shown to be non mutagenic in an in vitro bacterial mutation assay, non-clastogenic in an in vivo chromosome aberration assay and mouse micronucleus assay and did not induce DNA damage in a DNA repair test (NICNAS, 2001). Both lauramide and cocamide MEA have been reported to be negative in bacterial reverse mutation assays (CIR, 2015). Furthermore, the Optimised Approach based on Structural Indices Set - TIssue MEtabolism Simulator (OASIS-TIMES) for lauramide MEA predicts that the chemical would test negative for genotoxic potential in both in vitro (bacterial reverse mutation assay and chromosome aberration assay) and in vivo (micronucleus and liver clastogenicity assays).

Carcinogenicity

No animal data are available for the chemical. Based on the available genotoxicity data and QSAR modelling, the chemical is not considered to be carcinogenic. Experimental genotoxicity data indicated that related chemicals are not genotoxic (see Genotoxicity). The chemical and lauramide MEA have no structural alerts based on the mechanistic profilers of the OECD QSAR Application Toolbox v3.3.

Reproductive and Developmental Toxicity

No information is available for the chemical. Based on the limited data for a related chemical, there is no evidence that chemical would be a reproductive or developmental hazard.

In a combined reproduction and developmental study, repeated oral dosing for 55 days with PEG-4 rapeseedamide resulted in a no observed effect level (NOEL) for the parental generation and the offspring of 500 mg/kg bw/day (NICNAS, 2013).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation are local effects (skin and eye irritation). Adverse effects as a result of acute inhalation exposure cannot be ruled out.

Public Risk Characterisation

Based on the available international information, widespread cosmetic and domestic use is not expected.

If introduced into Australia, it is unlikely that cosmetic and personal care products would be formulated to be irritating; however, it is possible that domestic cleaning products may contain higher concentrations of the chemical. When high concentrations of the chemical are used in domestic products, irritant effects on exposure to concentrates could occur.

The concentration of the impurity 1,4-dioxane is restricted through listing in the Poisons Standard (SUSMP) in Schedule 6, with labelling requirements applying at above 100 ppm (Appendix G).

Overall, the public risk from the chemical is not considered to be unreasonable.

Occupational Risk Characterisation

During product formulation, dermal, ocular and inhalation exposure may occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

The chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine the appropriate controls.

The data available support an amendment to the hazard classification in the HSIS (Safe Work Australia) (refer to **Recommendation** section). However, should additional data on the irritation potential of a specific chemical under this CAS description become available, the classification can be revised based on the information.

NICNAS Recommendation

Assessment of the chemical is considered to be sufficient, provided that the recommended amendment to the classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

NICNAS recommends that formulators of products containing these chemicals should take into account the total surfactant concentration in the products when determining label instructions.

Regulatory Control

Public Health

Products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP, 2016).

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical and environmental hazards.

The CAS number represents chemicals with a range of ethoxylate units. An exemption to classification based on the number of ethoxylate units cannot be established based on the available data. If empirical data become available for a specific chemical under the CAS description indicating that a lower (or higher) classification is appropriate, these may be used to amend the default classification for that chemical.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Irritating to eyes (Xi; R36) Irritating to skin (Xi; R38)	Causes serious eye irritation - Cat. 2A (H319) Causes skin irritation - Cat. 2 (H315)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for consumers

Products containing the chemical should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from dermal, ocular and inhalation exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures that could minimise the risk include, but are not limited to:

- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

References

Approved Criteria for Classifying Hazardous Substances [NOHSC: 1008(2004)] Third edition. Accessed at http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/258/ApprovedCriteria_Classifying_Hazardous_Substances_NOHSC1008-2004_PDF.pdf

Ash M& Ash I 1997. Handbook of Industrial Surfactants Second Edition. Volume Two. Gower Publishing Limited.

Cosmetic Ingredient Review (CIR). 2015. Safety Assessment of Ethanolamides as Used in Cosmetics. International Journal of Toxicology. 34 (Supplement 1): 18S-34S.

European Commission Cosmetic Ingredients and Substances (CosIng) Database. Accessed May 2016 at http://ec.europa.eu/consumers/cosmetics/cosing/

Galleria Chemica. Accessed May 2016. http://jr.chemwatch.net/galleria/

Globally Harmonised System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third edition. Accessed at http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

Human& Environmental Risk Assessment on ingredients of European household cleaning products 2009. Alcohol Ethoxylates Human Health Risk Assessment. Accessed May 2013 at http://www.heraproject.com

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) 2001. New chemicals assessment report (Identity confidential)

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) Inventory Multi-tiered Assessment and Prioritisation (IMAP) Human Health Tier II Assessment for selected non-ionic surfactants - alkoxylate ethers of fatty alcohols. Accessed at www.nicnas.gov.au

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Full Public Report (2013). PEG-4 Rapeseedamide. Accessesd June 2016 at https://www.nicnas.gov.au/

Personal Care Products Council 2011. Compilation of Ingredients Used in Cosmetics in the United States, 1stEdition.

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed May 2016 at http://hsis.safeworkaustralia.gov.au/HazardousSubstance

Stepan Product Bulletin. Accessed online at: http://www.stepan.com/pdfs/Bulletins/NINOLL5.pdf

Substances in Preparations in Nordic Countries (SPIN). Accessed May 2016 at http://195.215.202.233/DotNetNuke/default.aspx

Test Facility (2014) 90-Day Oral Toxicity (Gavage) Study in the Wistar Rat. Unpublished report provided to NICNAS

Therapeutic Goods Administration–Department of Health 2016. Standard for the Uniform Scheduling of Medicines and Poisons No. 15 (the SUSMP 15). Accessed November 2016 at https://www.legislation.gov.au/Details/F2016L01638

United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) dictionary. Accessed May 2016 at http://gov.personalcarecouncil.org/jsp/gov/GovHomePage.jsp

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