File No: LTD/1670

October 2014

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

1-Propanaminium, 3-amino-N,N,N-trimethyl-, N-palm-oil acyl derivs., Me sulfates

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment.

For the purposes of subsection 78(1) of the Act, this Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This Public Report is also available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

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Director
NICNAS

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SUMMARY

The following details will be published in the NICNAS *Chemical Gazette:*

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/1670	Estee Lauder Pty Ltd	1-Propanaminium, 3-amino-N,N,N-trimethyl-, N-palm-oil acyl derivs., Me sulfates	ND*	≤ 1 tonne per annum	Component of cosmetic products

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical cannot be recommended for classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

Human health risk assessment
Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

When used at ≤ 3% in body lotions, ≤ 3.8% in hair styling products, ≤ 0.6% in other leave-on cosmetic products and ≤ 5% in rinse-off cosmetic products, the notified chemical is not considered to pose an unreasonable risk to public health.

Environmental risk assessment
On the basis of the PEC/PNEC ratio and the assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- No specific engineering controls, work practices or personal protective equipment are required for the safe use of the notified chemical itself. However, these should be selected on the basis of all ingredients in the formulation.

  Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

- A copy of the (M)SDS should be easily accessible to employees.

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Public Health

- When formulating cosmetic and personal care products containing the notified chemical, formulators should take into account its irritation potential.

Disposal

- Where reuse or recycling are unavailable or impracticable, dispose of the chemical in an environmentally sound manner in accordance with relevant Commonwealth, State, Territory and local government legislation.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
- the importation volume exceeds one tonne per annum notified chemical;
- the chemical is intended to use in aerosol spray cosmetics;
- the concentration of the notified chemical exceeds or is intended to exceed 3% in body lotions, 3.8% in hair styling products, 0.6% in other leave-on cosmetic products or 5% in rinse-off cosmetic products;
- additional information becomes available on the repeated dose toxicity potential of the notified chemical;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a component of cosmetic products, or is likely to change significantly;
- the amount of chemical being introduced has increased, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- 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.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

Material Safety Data Sheet
The MSDS of the notified chemical and products containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Estee Lauder Pty Ltd (ABN: 63 008 444 719)
165-175 Mitchell Road
Erskineville NSW 2043

NOTIFICATION CATEGORY
Limited-small volume: Chemical other than polymer (1 tonne or less per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
No details are claimed exempt from publication.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: all physico-chemical endpoints

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

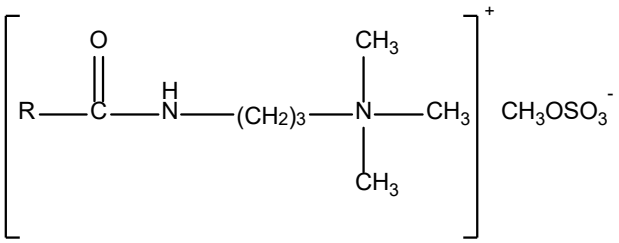
MARKETING NAME(S)
Incroquat Palm

CAS NUMBER
857026-47-2

CHEMICAL NAME
1-Propanaminium, 3-amino-*N,N,N*-trimethyl-, N-palm-oil acyl derivs., Me sulfates

MOLECULAR FORMULA
Unspecified

STRUCTURAL FORMULA



R = derived from fatty acids of palm oil

A typical distribution of the fatty acids in palm oil is C12:0 (0.2%), C14:0 (1.1%), C16:0 (44%), C16:1 (0.1%), C18:0 (4.5%), C18:1 (39.2%), C18:2 (10.1%), C18:3 (0.4%), C20:0 (0.4%) (CIR,2011).

MOLECULAR WEIGHT
Approximately 466-493 Da

ANALYTICAL DATA
Reference IR spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 99%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS

Chemical Name	1,3-Propanediamine, N,N-dimethyl-		
CAS No.	109-55-7	*Weight %*	< 0.001%
Hazardous Properties	Xn; R22 C; R34 R43 Conc. ≥ 25%: C; R34; R22; R43; ≥ 10% Conc. < 25%: C; R34; R43; ≥ 5% Conc. < 10%: Xi; R36/38; R43; ≥ 1% Conc. < 5%: Xi; R43.		

NON HAZARDOUS IMPURITIES (> 1% BY WEIGHT)
None

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: amber liquid

Property	Value	Data Source/Justification
Melting Point	339.87 °C* 349.84 °C**	Calculated (weighted value)
Boiling Point	772.46 °C* 799.24 °C**	Calculated (adapted Stein and Brown Method)
Density	Not determined	Imported in solution
Vapour Pressure	1.43×10^{-23} kPa at 25 °C* 1.39×10^{-24} kPa at 25 °C**	Calculated (modified Grain method)
Water Solubility	Not determined	The notified chemical is expected to disperse in water based on its surface activity.
Hydrolysis as a Function of pH	Not determined	The notified chemical contains hydrolysable functionally that is expected to slowly hydrolyse under environmental conditions (pH 4-9).
Partition Coefficient (n-octanol/water)	Not determined	The notified chemical is expected to partition to phase boundaries based on its surface activity.
Adsorption/Desorption	Not determined	Expected to sorb to soil, sediment and sludge due to its surface activity.
Dissociation Constant	Not determined	The notified chemical is a salt and is ionised in this form.
Surface Tension	37.1 mN/m	Measured
Particle Size	Not determined	Liquid
Flash Point	Not determined	Imported in solution
Flammability	Not determined	Imported in solution
Autoignition Temperature	Not determined	Imported in solution
Explosive Properties	Not determined	Contains no functional groups that imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that imply oxidative properties

* For the notified chemical containing the fatty acid chain C16:0
**For the notified chemical containing the fatty acid chain C18:1

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties, refer to Appendix A.

Reactivity
The notified chemical is expected to be stable under normal conditions of use.

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is not recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported in finished cosmetic products at up to 5% concentration.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	1	1	1	1	1

PORT OF ENTRY
Sydney by wharf

IDENTITY OF MANUFACTURER/RECIPIENTS
Estee Lauder Pty Ltd

TRANSPORTATION AND PACKAGING
The products containing the notified chemical (at up to 5% concentration) will be imported in containers suitable for retail sale (e.g. 200 mL). These will be packaged in cardboard cartons. The cartons will be distributed within Australia by road.

USE
The notified chemical will be used as a component of cosmetic products at up to 5% concentration. The content in the final consumer products will vary, with the following proposed usage concentrations: body lotions (≤ 3%), hair styling products (≤ 3.8%), other leave-on cosmetic products (≤ 0.6%), and rinse-off cosmetic products (≤ 5%).

OPERATION DESCRIPTION
The notified chemical will be imported as a component of finished cosmetic products. Reformulation will not take place in Australia.

The finished products containing the notified chemical will be used by consumers and professionals (such as workers in beauty salons). Application of products could be by hand or through the use of an applicator.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and storage	4	12
Store persons	4	12
Salon workers	8	260

EXPOSURE DETAILS

Transportation and storage workers may only be exposed to the notified chemical as a component of end-use products (at up to 5% concentration) in the unlikely event of an accident.

Exposure to the notified chemical in end-use products may occur in professions where the services provided involve the application of cosmetic products to clients (e.g. workers in beauty salons). Such professionals may use some personal protective equipment (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 products containing the notified chemical.

6.1.2. Public Exposure

There will be widespread and repeated exposure of the public to the notified chemical (at ≤ 5% concentration) through the use of the cosmetic products. The principal route of exposure will be dermal.

Data on typical use patterns of cosmetic categories in which the notified chemical may be used are shown in the following tables (SCCS, 2012; Cadby *et al.*, 2002). For the purposes of the exposure assessment via the dermal route, Australian use patterns for the various product categories are assumed to be similar to those in Europe. Based on the physico-chemical properties of the notified chemical and dermal absorption data for analogue chemicals (see Section 6.2, Toxicokinetics), dermal absorption of 10% was used for calculation purposes. An adult average bodyweight of 60 kg was used for the calculations.

Cosmetic products (dermal exposure):

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (mg/kg bw/day)
Body lotion	7820	3	1	0.391
Face cream	1540	0.6	1	0.015
Hand cream	2160	0.6	1	0.022
Hair styling products	4000	3.8	0.1	0.025
Make-up remover	5000	5	0.1	0.042
Shower gel	18670	5	0.01	0.016
Hand wash soap	20000	5	0.01	0.017
Shampoo	10460	5	0.01	0.009
Hair conditioner	3920	5	0.01	0.003
Facial cleanser	800	5	0.01	0.001
Total				**0.54**

C = concentration; RF = retention factor.
Daily systemic exposure = Amount × C (%) × RF × dermal absorption (%)/body weight (60 kg)

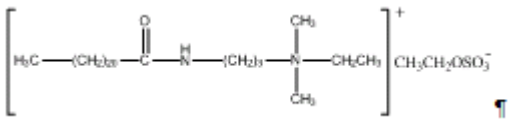
The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above table that contain the notified chemical. This would result in a combined internal dose of 0.54 mg/kg bw/day.

6.2. Human Health Effects Assessment

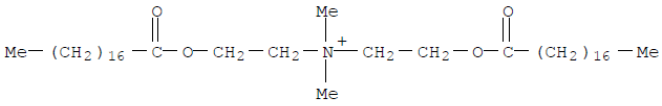
The results from toxicological investigations conducted on the notified chemical and suitable analogues are summarised in the table below. For full details of the studies on the notified chemical and analogue 1, refer to Appendix B.

The identity of the analogues is as follows:

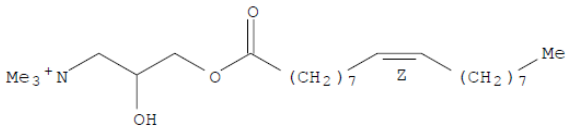
Analogue 1
Chemical name: 1-Propanaminium, N-ethyl-N,N-dimethyl-3-[(1-oxodocosyl)amino]-, ethyl sulfate (1:1)
CAS number: 68797-65-9



Analogue 2
Chemical name: Ethanaminium, N,N-dimethyl-2-[(1-oxooctadecyl)oxy]-N-[2-[(1-oxooctadecyl)oxy]ethyl]-, chloride (1:1)
CAS Number: 67846-68-8
Structure:

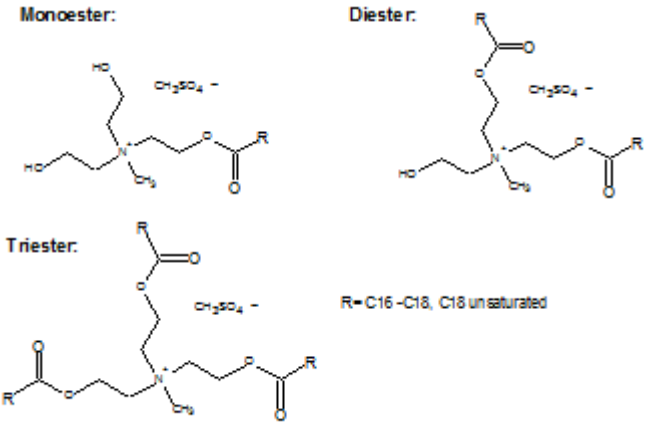


Analogue 3
Chemical name: (Z)-2-hydroxy-3-[(1-oxo-9-octadecenyl)oxy]propyltrimethylammonium chloride
CAS Number: 19467-38-0
Structure:



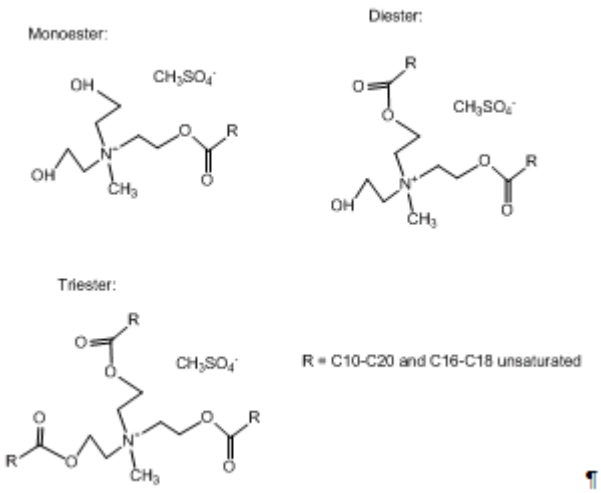
Analogue 4
Chemical name: Ethanaminium, 2-hydroxy-N,N-bis(2-hydroxyethyl)-N-methyl-, esters with C16-18 and C18-unsatd. fatty acids, Me sulfates (salts)
CAS Number: 157905-74-3

Structure:



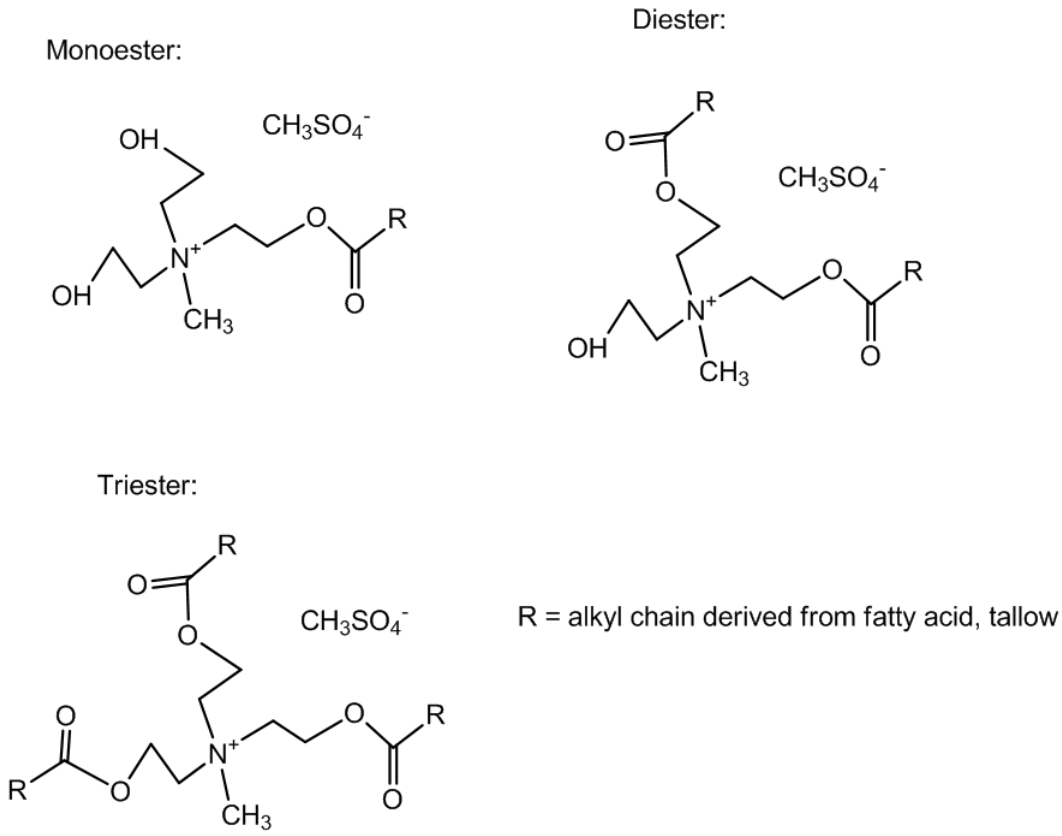
Analogue 5
Chemical name: Fatty acids, C10-20 and C16-18-unsatd., reaction products with triethanolamine, di-Me sulfate-quaternized
CAS Number: 91995-81-2

Structure:



Analogue 6
Chemical name: Fatty acids, tallow, reaction products with triethanolamine, di-Me sulfate-quaternized
CAS Number: 93334-15-7

Structure:



Justification for the analogues
Similar to the notified chemical analogues 1-6 are cationic surfactants comprised of a quaternary ammonium group and fatty acid side chains of similar length. Both the notified chemical and analogues 1, 4, 5 and 6 have methyl sulfate as the counterion whereas analogues 2 and 3 have chloride as the counterion. The nature of the counterion is not expected to have a significant contribution to the hazardous properties of the chemical.

Given the analogues belong to the same class of compounds as the notified chemical and contain all the same functional groups expected to contribute to any hazardous properties, the analogue chemicals are considered to give a reasonable indication of the toxicological properties of the notified chemical.

Endpoint	*Test substance*	*Result and Assessment Conclusion*
Rat, acute oral toxicity	Analogue 5	LD50 > 2,000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	Analogue 4	LD50 > 2,000 mg/kg bw; low toxicity
	Analogue 5	LD50 > 2,000 mg/kg bw; low toxicity
Skin irritation (in vitro)	Notified chemical	irritating
Eye irritation (in vitro) (≤ 5%)	Notified chemical	irritating
Eye irritation (in vitro)	Analogue 1	non-irritating
Human, skin sensitisation – RIPT (4%)	Notified chemical	no evidence of sensitisation
Human, skin sensitisation – RIPT (5%)	Notified chemical	no evidence of sensitisation
Rat, repeat dose oral (gavage) toxicity – 28 days.	Analogue 4	NOAEL > 800 mg/kg bw/day
Rat, repeat dose oral (gavage) toxicity – 90 days.	Analogue 6	NOEL = 300 mg/kg bw/day
Genotoxicity – in vitro mammalian chromosome aberration test (chinese hamster V79 Cells)	Analogue 4	non genotoxic
Genotoxicity – in vitro mammalian forward mutation assay (mouse lymphoma L578Y cells)	Analogue 2	non genotoxic
Genotoxicity – in vivo mammalian mouse micronucleus Test	Analogue 5	non genotoxic
Developmental effects	Analogue 2	NOAEL > 1,000 mg/kg bw/day
	Analogue 3	NOAEL > 1,000 mg/kg bw/day

Toxicokinetics

Toxicokinetic data on the notified chemical was not provided. The moderately high molecular weight and ionic character of the notified chemical suggests that absorption across the lipid rich environment of the stratum corneum into the epidermis would be slow. This hypothesis is supported by dermal toxicokinetic studies on analogue chemicals. In *in vivo* studies using ^{14}C radio labelling in rats under occlusive conditions, analogue 3 showed absorptions of 0.7% and 2% depending on the position of the ^{14}C atom in the analogue (HERA, 2009). In addition, a similar quaternary ammonium compound, cetrimonium bromide (CAS No. 57-09-0), was indicated to be poorly absorbed in a percutaneous study in rats (CIR, 2010). The study showed that 0.59% of 1% cetrimonium bromide penetrated rat skin after 15 min; 0.93% of 0.5% cetrimonium bromide in a hair rinse formulation penetrated after 5 minutes exposure followed by rinsing; and 3.15% of 3.0% cetrimonium bromide in water penetrated after 15 minutes exposure.

Acute toxicity

The acute oral toxicity of analogue 5 was shown to be low based on studies in rats (HERA, 2009). The acute dermal toxicity of analogues 4 and 5 was shown to be low based on studies in rats (HERA, 2009). Based on the results from these analogues the notified chemical is not expected to be acutely toxic via the oral and dermal route. There is no data available on the inhalation toxicity of the notified chemical or suitable analogues.

Irritation

The notified chemical has a quarternary ammonium functional group which is a structural alert for corrosion (Hulzebos et al., 2005 and Tsakovska et al., 2007).

The notified chemical was irritating under the conditions of an *in vitro* skin (Epiderm™ Human Dermal Epithelial Model) irritation study and was determined to be moderately irritating at 5% concentration in an *in vitro* eye (HET-CAM) irritation study. However, analogue 1 was not irritating in an *in vitro* eye (Matrix™ toxicity testing system) irritation study.

Based on the available information, the notified chemical is expected to be irritating to the skin and eye. The potential for the notified chemical to be severely irritating to eyes cannot be ruled out.

Sensitisation

The notified chemical tested as a 5% aqueous solution and in a formulation at 4% concentration was not sensitising to the skin in human repeat insult patch studies.

Repeated dose toxicity
A 28 day repeated dose oral toxicity study in rats with analogue 4 gave a NOAEL of > 800 mg/kg bw/day. No mortality, morbidity or significant changes of any of the investigated parameters were noted (HERA, 2009).

The subchronic toxicity of analogue 6 was evaluated in an oral gavage study at dose levels of 0, 100, 300 or 1000 mg/kg bw/day (HERA, 2009). Animals of the high dose groups displayed potentially substance related increases of blood liver enzymes, signs of gastric irritation and regressive epithelial changes in the bladder. However it is noted that the interpretation of the study results was hampered due to occurrence of a bacterial infection in all dose groups and the test substance was not fully characterised. A NOEL of 300 mg/kg bw/day was assigned by the study authors.

In the absence of adequate data on the chronic toxicity of the notified chemical, data on analogue 6 will be used to conduct the quantitative risk assessment, i.e., the notified chemical is not expected to cause adverse effects as a result of repeated oral exposure to doses of up to 300 mg/kg bw/day.

Mutagenicity/Genotoxicity
No genotoxic effects were seen in 2 different *in vitro* studies and 1 *in vivo* study (which included evidence that the test substance reached the bone marrow) involving analogues 2, 4 and 5 (HERA, 2009). The notified chemical is not expected to be genotoxic based on the results of these studies.

Developmental Toxicity
Two studies (one using analogue 2 and the other analogue 3) have been conducted where female rats were orally dosed at concentrations of up to 1,000 mg/kg bw/day from day 6 to 15 post mating before being sacrificed on day 21 (HERA, 2009). A slight but statistically significant post-implantation loss was noted with analogue 2 in the high dose group, although the rate was still within that seen in the historical controls. No other adverse effects were noted in either study and hence the NOAEL was the highest dose tested. The notified chemical is not expected to cause teratogenic effects based on the results of the studies conducted using analogues 2 and 3.

Health hazard classification
Based on the available information, the notified chemical cannot be recommended for classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Beauty care professionals may come into contact with products containing the notified chemical at ≤ 5% concentration. These products will also be available to the public. The risk to workers who regularly use these products is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified chemical (for details of the public health risk assessment, see Section 6.3.2).

6.3.2. Public Health
Members of the public may experience repeated exposure to the notified chemical (at ≤ 5% concentration) through the use of the cosmetic products.

Repeated dose toxicity
The repeat dose toxicity potential was estimated by calculation of the margin of exposure (MoE) of the notified chemical using the worst case exposure scenario from use of multiple products (see Section 6.1.2). A person who uses all the products simultaneously would result in a combined systemic internal dose of 0.54 mg/kg bw/day of the notified chemical. Using a NOEL of 300 mg/kg bw/day, which was derived in a 90-day repeated dose oral toxicity study on an analogue chemical (analogue 6), the margin of exposure (MoE) was estimated to be 556. A MoE value ≥ 100 is considered to be acceptable to account for intra- and inter-species differences. Therefore the MoE is considered acceptable.

The repeated dose toxicity effects of the notified chemical have not been determined. It is acknowledged that there is some uncertainty in the estimated MOE, due to the use of the NOEL for analogue 6 derived from a study with some reported deficiencies.

Irritation
The notified chemical is likely to be irritating to the skin and potentially severely irritating to eyes. Skin irritation effects are not expected from use of the notified chemical at the proposed use concentrations in cosmetic products. However, the potential for eye irritancy is of concern, particularly with rinse-off products (up to 5% notified chemical). Due to the reduced contact time likely associated with rinse-off products (containing the notified chemical at up to 5%) and the likely dilution of products with water at the time of eye contact, the extent of irritation should be reduced. The potential for eye irritation may be further minimised by the inclusion of appropriate labelling and directions for use to warn against eye contact. Therefore, the risk to the public from possible irritancy of products containing the notified chemical at up to 5% is not considered to be unreasonable.

Sensitisation
Methods for the quantitative risk assessment for dermal sensitisation have been proposed and been the subject of significant discussion (see for example, Api *et al.*, 2008 and RIVM, 2010). As is shown in the table below, the Consumer Exposure Level (CEL) from use of the notified chemical in a number of different cosmetic products may be estimated (SCCS, 2010; RIVM, 2006). When tested at 4% and 5% concentration in human repeat insult patch studies, the notified chemical was determined by the study authors to not be a skin sensitiser. Consideration of the details of the studies, and application of appropriate safety factors, allowed the derivation of an Acceptable Exposure Level (AEL) of 15 μg/cm^2 (derived from the study conducted at 4% concentration). In this instance, the factors employed included an intraspecies factor (10), a matrix factor (1), a use and time factor (3.16) and a database uncertainty factor (3.16), giving an overall safety factor of ~100.

Product type	**Proposed usage concentration (%)**	**CEL chemical** (μg/cm^2)	**AEL chemical** (μg/cm^2)	**Recommended usage concentration (%)**
Body lotion	≤ 3	14.97	15	≤ 3
Hair styling products	≤ 3.8	15.05	15	≤ 3.8
Other leave-on cosmetics (assumed: face cream)	≤ 0.6	16.35	15	≤ 0.6
Rinse-off cosmetics (assumed: hand wash soap)	≤ 5	11.63	15	≤ 6.5

As the proposed usage concentration is within the recommended usage concentration, the risk to the public of the induction of sensitisation that is associated with the use of the notified chemical in body lotions (at ≤ 3%), hair styling products (at ≤ 3.8%), other leave-on cosmetic products (using face cream as a worst case example; at ≤ 0.6%), and rinse-off cosmetic products (using hand wash soap as a worst case example; at ≤ 5%) is not considered to be unreasonable. It is acknowledged that consumers may be exposed to multiple products containing the notified chemical, and a quantitative assessment based on the aggregate exposure has not been conducted.

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at 3% in body lotions, 3.8% in hair styling products, 0.6% in other leave-on cosmetic products and 5% in rinse-off cosmetic products is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The notified chemical will not be manufactured, reformulated or repackaged in Australia. Therefore, there will be no release of the notified chemical to the environment from these activities.

RELEASE OF CHEMICAL FROM USE
The majority of the annual import volume of the notified chemical is expected to be released to sewers based on its use as a component as cosmetic products.

RELEASE OF CHEMICAL FROM DISPOSAL

Notified chemical residues in empty containers and expired material containing the notified chemical are expected to be disposed of to landfill along with containers or washed to sewers when containers are rinsed with water before the recycling of the containers.

7.1.2. Environmental Fate

No environmental fate data were submitted. The notified chemical is a cationic surfactant belonging to a quaternary ammonium category. Most surfactants in this group were determined to be biodegradable (Madsen et al, 2001). The notified chemical is expected to have a similar degradation pathway as the chemicals in this category and is expected to undergo some extent of degradation in the environment.

The majority of the notified chemical is expected to be released to sewage treatment plants (STPs) via domestic wastewater. Due to its cationic functional group and surface activity, a significant amount of the notified chemical is expected to sorb to sludge in STPs. The sludge containing notified chemical residues may be sent to landfill or applied to soils for land remediation. Notified chemical released to surface waters is expected to partition to suspended solids and organic matter, and disperse. Consequently, the notified chemical is not expected be significantly bioavailable. The notified chemical is a cationic surfactant and is unlikely to cross the lipid cell membrane and therefore, is not expected to bioaccumulate. The notified chemical is expected to ultimately degrade biotically and/or abiotically to form water and oxides of carbon, nitrogen and sulphur.

7.1.3. Predicted Environmental Concentration (PEC)

The calculation for the Predicted Environmental Concentration (PEC) is summarised in the table below. Based on the reported use, it is assumed that 100% of the total import volume of the notified chemical is released to sewers on a nationwide basis over 365 days per year. It is evidenced by literature data that more than 99% of a representative chemical in this chemical category is expected to adsorb to waste water solids within 30 minutes of initial exposure (Larry et al, 1982). Therefore, the PEC for the notified chemical has been calculated assuming that 99% of the notified chemical will be removed during STP processes.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	99%	**Mitigation**
Daily effluent production:	4,523	ML
Dilution Factor - River	1	
Dilution Factor - Ocean	10	
PEC - River:	0.006	µg/L
PEC - Ocean:	0.0006	µg/L

Partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 6 mg/kg (dry wt). Biosolids are applied to agricultural soils, with an assumed average rate of 10 t/ha/year. Assuming a soil bulk density of 1500 kg/m^3 and a soil-mixing zone of 10 cm, the concentration of the notified chemical may approximate 0.04 mg/kg in applied soil. This assumes that degradation of the notified chemical occurs in the soil within 1 year from application. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated biosolids application, the concentration of notified chemical in the applied soil in 5 and 10 years may approximate 0.2 mg/kg and 0.4 mg/kg, respectively.

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.006 µg/L may potentially result in a soil concentration of approximately 0.04 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the

concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 0.2 µg/kg and 0.4 µg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity data were provided for the notified chemical. The notified chemical is a cationic surfactant. Cationic chemicals are known to be toxic to aquatic life. The range of the ecotoxicological results for fish, daphnia and algae measured for surfactants in the quaternary ammonium group are expected to be indicative of the toxicity of the notified chemical. The results from ecotoxicological investigations for the analogue chemicals, as summarised in the table below, were available in a reliable peer reviewed document (Madsen et al, 2001).

Endpoint	Result	Assessment Conclusion
Fish acute toxicity	LC50 = 0.36 - 7.0 mg/L	May be very toxic to fish
Daphnia acute toxicity	EC50 = 0.1 -18 mg/L	May be very toxic to aquatic invertebrates
Algal acute toxicity	EC50 = 0.03 - 18 mg/L	May be very toxic to algae

The notified chemical and the analogues can be considered to belong to similar cationic surfactant groups based on their functional groups. Therefore, the ecotoxicological endpoints measured for the analogues are considered acceptable for the purpose of regulatory risk assessment. However, as the toxicity of these surfactants is expected to vary with surfactant tail length and structure, these endpoints are not expected to be entirely representative for the purposes of classification under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009). Therefore, the notified chemical is not formally classified for its acute and chronic hazard under the GHS.

7.2.1. Predicted No-Effect Concentration

For the worst case scenario, the Predicted No-Effect Concentration (PNEC) was calculated using the most conservative toxicity endpoint (algae, EC50 = 0.03 mg/L) for an analogue substance and an assessment factor of 1000. The conservative assessment factor of 1000 was used since the analogue ecotoxicity endpoints were used in lieu of the measured data for the notified chemical.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (algae)	0.03	mg/L
Assessment Factor	1000	
PNEC:	0.03	µg/L

7.3. Environmental Risk Assessment

Risk Assessment	***PEC µg/L***	***PNEC µg/L***	***Q***
Q - River:	0.006	0.03	0.2
Q - Ocean:	0.0006	0.03	0.02

The Risk Quotients (Q = PEC/PNEC) for a conservative discharge scenario have been calculated to be less than 1 for both riverine and marine compartment. Although the notified chemical may be toxic to aquatic species based on the analogue data, it is unlikely to reach ecotoxicologically significant concentrations in the environment based on the assessed use pattern. Furthermore, the notified chemical is not expected to bioaccumulate in biota due to its surface activity and cationicity. On the basis of the assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Surface Tension 37.1 mN/m

Method	In house method
Remarks	The test was conducted on a 0.1% solution of the test material using a Kruss K 100SF Tension meter.
Test Facility	Croda (2013)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Irritation – skin (in vitro)

TEST SUBSTANCE: Notified chemical

METHOD: The MatTek Corporation EpiDerm™ Skin Model In Vitro Toxicity Testing System

Vehicle: None

Remarks - Method: Cell viability is determined by the activity of mitochondrial succinate dehydrogenase, which reduces a yellow, water-soluble, tetrazolium salt to a purple, insoluble formazan derivative. The amount of reduction is determined by spectrophotometry.

The cell layer is incubated with test substance and controls in microplates, extracted and the absorbance read at 570 nm. Distilled water was used as the negative control.

RESULTS

Test material	*System*	*Percent viability (%)*	*Percent inhibition (%)*
100% - 1 hr	EpiDerm	54	46
100% - 4.5 hr	EpiDerm	18	82
100% - 20 hr	EpiDerm	12	88

Remarks - Results: The ET-50 is a measure of 50% cell viability. The test substance elicited an ET-50 of 1.2 hours, which according to the MatTek corporation irritation guidelines corresponds to an in vivo dermal irritancy potential in the moderately irritating range, similar to 1% sodium dodecyl sulfate.

CONCLUSION: The notified chemical was irritating to the skin under the conditions of the test.

TEST FACILITY: Consumer Product Testing (2005a)

B.2. Irritation – eye (in vitro)

TEST SUBSTANCE: Notified chemical

METHOD: The Hen's Egg Test-Utilising the Chorioallantoic Membrane (HET-CAM)

Vehicle: Distilled water

Remarks - Method: No protocol deviations were reported.

RESULTS

Test material	*Average score*
Distilled water	1.75
Notified chemical (5%)	13.75
Notified chemical (2.5%)	10.00
Notified chemical (1%)	10.75

Remarks - Results: The results indicated that at 5% would have a moderate irritation potential *in vivo* and at 2.5% and 1% would have a moderate to slight irritation potential *in vivo*.

CONCLUSION: The notified chemical was irritating to eyes under the conditions of the test.

TEST FACILITY: Consumer Product Testing (2005b)

B.3. Irritation – eye (in vitro)

TEST SUBSTANCE	Analogue 1
METHOD	The Matrex™ *In Vitro* Toxicity Testing System
Vehicle	Not reported
Remarks - Method	The procedure involves a solubilised, reactive tetrazolium salt (MTT), which was metabolised by the mitochondria of living cells and converted to a purple formazan dye. The colour intensity of the skin replica extract, measured photometrically (the absorbance of each extract was determined at 570 nm), correlated directly with its viability. When measured against controls, vales ranging from 0% to 100% (plus or minus approximately 20%) could be calculated for each dose of applied substance.

RESULTS

Test material	*System*	*Percent viability (%)*	*Percent inhibition (%)*
100% - 1 hr	Living Skin Equivalent (LSE)™	81	19
10% - 1 hr	Living Skin Equivalent (LSE)™	88	12
1% - 1 hr	Living Skin Equivalent (LSE)™	93	7

Remarks - Results	The test substance elicited *in vitro* irritation potential compared to that recorded for propylene glycol.
CONCLUSION	The notified chemical was considered to be non-irritating to the eye under the conditions of the test.
TEST FACILITY	Consumer Product Testing (1992)

B.4. Skin sensitisation – human volunteers

TEST SUBSTANCE	Notified chemical (5% aqueous solution)
METHOD	Repeated insult patch test with challenge
Study Design	Induction Procedure: patches infused with 0.2 mL test substance were applied 3 times per week on Mondays, Wednesdays and Fridays for a total of 9 applications. Patches were removed after 24 h and graded after an additional 24 h (or 48 h for patches applied on Friday). Rest Period: ~2 weeks Challenge Procedure: identical patches were applied to a naïve site next to the original induction patch site. Patches remained in place for 24 h. Sites were graded 24 and 72 h post-patch removal.
Study Group	47 F, 14 M; age range 16-74 years
Vehicle	None
Remarks - Method	Semi-occluded. The test substance was spread on a 2.5 cm × 2.5 cm patch. Eleven subjects discontinued for various reasons, none of which were related to the application of the test substance.
RESULTS	
Remarks - Results	50/61 subjects completed the study. It was reported that the subjects discontinued for various reasons, none of which were related to the application of the test substance. No adverse responses were noted during induction or challenge.
CONCLUSION	The test substance was non-sensitising under the conditions of the test.
TEST FACILITY	Consumer Product Testing (2005c)

B.5. Skin sensitisation – human volunteers

TEST SUBSTANCE	Formulation containing 4% notified chemical
METHOD	Repeated insult patch test with challenge
Study Design	Induction Procedure: patches infused with 150 µL test substance were applied 3 times per week on Mondays, Wednesdays and Fridays for a total of 9 applications. Patches were removed after 24 h and graded after an additional 24 h (or 48 h for patches applied on Friday). Rest Period: 7 days Challenge Procedure: identical patches were applied to original sites and naïve sites. Patches remained in place for 24 h. Sites were graded at patch removal and 24 h post-patch removal.
Study Group	84 F, 23 M; age range 18-65 years
Vehicle	None
Remarks - Method	Semi-occluded. The test substance was spread on a 2 cm × 2 cm patch.
RESULTS	
Remarks - Results	In the induction phase, no responses were noted in 101/107 subjects. Faint redness was observed in the remaining 6 subjects. No adverse responses were noted during the challenge phase in the 103 subjects that completed this phase.
CONCLUSION	The test substance was non-sensitising under the conditions of the test.
TEST FACILITY	Product Investigations (2006)

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