File No: LTD/1940

December 2016

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Beeswax, ethoxylated

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 and Energy.

This Public Report is 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/1940	Revlon Australia Pty Ltd And Ozdare Business Services Pty Ltd	Beeswax, ethoxylated	ND*	≤ 1 tonne/s per annum	Cosmetic ingredient

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified polymer is not recommended for classification according to the *Globally Harmonised System of 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 in the proposed manner, 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 reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical during reformulation processes:
  - Avoid contact with skin and eyes

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical during reformulation processes:
  - Coveralls, impervious gloves, goggles

  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 of 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.

Disposal

- Where reuse or recycling are not appropriate, dispose of the notified chemical in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

Emergency procedures

- Spills and/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 concentration of the notified chemical exceeds or is intended to exceed 12% in cosmetic products;
- the notified chemical is intended for use as primary ingredient in sunscreen products.

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a cosmetic ingredient, 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 (M)SDS of the notified chemical and a product containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Revlon Australia Pty Ltd (ABN: 18 095 360 731)
12 Julius Avenue
NORTH RYDE NSW 2113

Ozdare Business Services Pty Ltd (ABN: 32 122 738 836)
7 Endeavour Way
SUNSHINE WEST VIC 3020

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 for all physico-chemical endpoints.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None.

NOTIFICATION IN OTHER COUNTRIES
None.

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Apifil® CG (cosmetic grade)

CAS NUMBER
385815-07-6

CHEMICAL NAME
Beeswax, ethoxylated

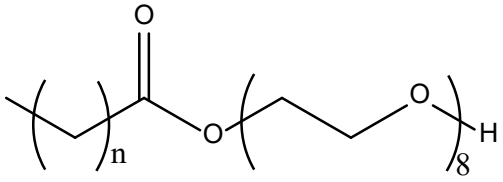
OTHER NAME
PEG-8 Beeswax

MOLECULAR FORMULA
Unspecified

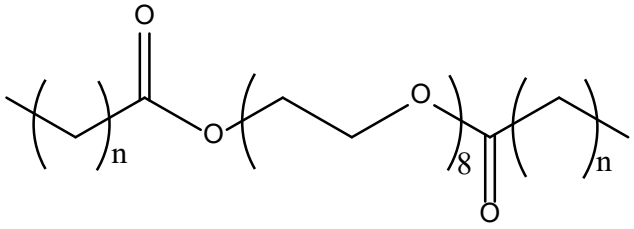
STRUCTURAL FORMULA

The notified chemical is a mixture of several molecules:

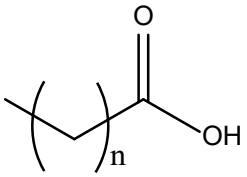
- *monoesters of PEG-8 and fatty acids (where n = 14 - 32)*



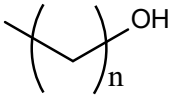
- *diesters of PEG-8 and fatty acids (where n = 14 - 32)*



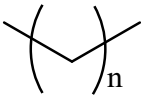
- *free fatty acids (where n = 14 - 32)*



- *free fatty alcohols (where n = 23 - 31)*



- *aliphatic hydrocarbons (where n = 21 - 31)*



Beeswax is a UVCB, and contains components that are not expected to react with the PEG groups present. The notifier has indicated that the introduced chemical will predominantly have a polyethylene glycol (PEG) component of eight monomers. However, the CAS name that is being notified allows for a range of PEG chain lengths and subsequently PEG-8 beeswax is only a subset of the notified chemical and has therefore been treated as an analogue.

MOLECULAR WEIGHT
> 500 Da

ANALYTICAL DATA
Reference IR spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
100% (as a UVCB)

NON HAZARDOUS (> 1% BY WEIGHT) AND HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None identified.

ADDITIVES/ADJUVANTS
None.

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Semi-solid wax

Property	Value	Data Source/Justification
Melting Point/Freezing Point	62-66 °C	Analogue 1
Boiling Point	> 250 °C at 101.3 kPa	Analogue 3
Density	0.95 – 0.97 kg/m^3 at 15 °C	Analogue 1
Vapour Pressure	Not determined	Expected to be very low based on molecular weight
Water Solubility	Insoluble	Analogue 3
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionalities; however, not expected to rapidly hydrolyse under environmental conditions (pH 4-9)
Partition Coefficient (n-octanol/water)	log Pow = 5.34	Analogue 2. Calculated using KOCWIN v2.0 (US EPA, 2012).
Adsorption/Desorption	Not determined	The notified chemical is an emulsifier and is expected to adsorb to soil and sediment.
Dissociation Constant	Not determined	The notified chemical does not contain any functional groups that are expected to dissociate in water.
Flash Point	> 170 °C	Analogue 3
Flammability	Not determined	Not expected to be flammable based on flash point.
Autoignition Temperature	> 300 °C	Analogue 3
Explosive Properties	Not determined	Not expected to be explosive based on chemical structure.
Oxidising Properties	Not determined	Not expected to be oxidative based on chemical structure.

Analogue 1 - Beeswax
Analogue 2 PEG-8 Stearate
Analogue 3 – PEG-8 Beeswax

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 of 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 not be manufactured in Australia. The notified chemical will be imported into Australia either in neat form for formulation into cosmetic products or as a component of end-use products (at concentrations ≤ 12%).

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
Melbourne and Sydney

IDENTITY OF MANUFACTURER
Gattefossé SAS, France

TRANSPORTATION AND PACKAGING
The notified chemical may be imported into Australia in its neat form as semi-solid pellets packaged in 25 kg bags in cartons, or as a component of finished cosmetic products at ≤ 12% concentration. Finished cosmetic products containing the notified chemical will be packaged in plastic bottles (≤ 500 mL) or tubes for retail sale.

USE
The notified chemical will be used as an ingredient in a variety of rinse-off and leave-on cosmetic products at concentrations of ≤ 12%.

OPERATION DESCRIPTION
The notified chemical will be imported in its neat form for formulation of cosmetic products, or as a component of finished cosmetic products (at ≤ 12% concentration) which will be sold to the public in the same form in which they are imported.

Reformulation
The procedures for incorporating the notified chemical (in its neat form) into end-use products will vary depending on the nature of the cosmetic product being formulated and both manual and automated steps will likely be involved. However, in general, it is expected that for the reformulation process, the notified chemical will be weighed and added to the mixing tank where it will be blended with additional additives to form the finished cosmetic products. This will be followed by automated filling of the reformulated products into containers of various sizes. The blending operations are expected to be highly automated and use closed systems and/or adequate ventilation. During the formulation process, samples of the notified chemical and the finished cosmetic products will be taken for quality control testing.

End-use
Finished cosmetic products containing the notified chemical at ≤ 12% concentration will be used by consumers and by professionals such as hairdressers and workers in beauty salons. Depending on the nature of the product, application of products could be by hand, sprayed 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)*
Warehouse and Transport	4	12
Compounder	8	12
Chemist	3	12
Processing	8	12
End-users	8	365

EXPOSURE DETAILS
Transport, storage and retail workers may come into contact with the notified chemical in its neat form, or at ≤ 12% concentration only in the event of accidental rupture of packages.

Reformulation
During reformulation into cosmetic products, dermal, ocular and inhalation exposure of workers to the notified chemical in its neat form may occur. Exposure is expected to be minimised through the use of exhaust ventilation and/or automated/enclosed systems as well as through the use of personal protective equipment (PPE) such as coveralls, eye protection, impervious gloves and respiratory protection (as appropriate).

End-use

Exposure to the notified chemical at ≤ 12% concentration 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). The principal route of exposure will be dermal, while oral and ocular exposure is also possible. Such professionals may use some 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 customers 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 through the use of a wide range of cosmetic products (at ≤ 12% concentration in individual products). The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if the products are applied by spray.

Data on typical use patterns of product categories in which the notified chemical may be used are shown in the following tables (SCCS, 2012; Cadby *et al.*, 2002; ACI, 2010; Loretz *et al.,* 2006). 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. In the absence of dermal absorption data, a dermal absorption (DA) of 10% was assumed for the notified chemical (CIR, 2010). For the inhalation exposure assessment, a 2-zone approach was used (Steiling *et al*., 2014; Rothe *et al*., 2011; Earnest, Jr, 2009). An adult inhalation rate of 20 m^3/day (enHealth, 2012) was used and it was conservatively assumed that the fraction of the notified chemical inhaled is 50%, with the reminder ending up, as intended, on the hair. A lifetime average female body weight (BW) of 64 kg (enHealth, 2012) was used for calculation purposes.

Product type	Amount (mg/day)	C (%)	Retention Factor (RF) (unitless)	Daily systemic exposure (mg/kg bw/day)
Body lotion	7820	12	1	1.4663
Face cream	1540	12	1	0.288
Hand cream	2160	12	1	0.4050
Fine fragrances	750	12	1	0.1406
Deodorant (non-spray)	1500	12	1	0.2813
Shampoo	10460	12	0.01	0.0196
Conditioner	3920	12	0.01	0.0074
Shower gel	18670	12	0.01	0.0350
Hand wash soap	20000	12	0.01	0.0375
Hair styling products	4000	12	0.1	0.0750
Foundation	510	12	1	0.0956
Mascara	25	12	1	0.0047
Eyeliner	5	12	1	0.0009
Eye shadow	20	12	1	0.0038
Make up remover	5000	12	0.1	0.0938
Total				**2.9545**

C = concentration of the notified chemical; RF = retention factor.
Daily systemic exposure = (Amount × C × RF × DA)/BW

Aerosol products (Inhalation exposure)

Product type	Amount (g/day)	C (%)	Inhalation Rate (m^3/day)	Exposure Duration (Zone 1) (min)	Exposure Duration (Zone 2) (min)	Fraction Inhaled (%)	Volume (Zone 1) (m^3)	Volume (Zone 2) (m^3)	Daily systemic exposure (mg/kg bw/day)
Hairspray	9.89	12	20	1	20	50	1	10	0.3863

Daily systemic exposure = [(Amount × C × Inhalation Rate × Fraction Inhaled × 0.1) / BW × 1440)] × [Exposure Duration (Zone 1)/Volume (Zone 1) + Exposure Duration (Zone 2)/Volume (Zone 2)]

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above tables that contain the notified chemical. This would result in a combined internal dose of 3.3408 mg/kg bw/day. It is acknowledged that inhalation exposure to the notified chemical from use of other cosmetic and household products may occur. However, it is considered that the combination of the conservative (screening level) hair spray inhalation exposure assessment parameters, and the aggregate exposure from use of the dermally applied products, which assumes a conservative 10% absorption rate, is sufficiently

protective to cover additional inhalation exposure to the notified chemical from use of other spray cosmetic products with lower exposure factors.

6.2. Human Health Effects Assessment

No toxicity data were submitted for the notified chemical. Data on a range of analogues that are component of the notified chemical has instead been used to estimate the human health effects. Analogue 1 (beeswax), Analogue 3 (PEG-8, beeswax) and Analogue 4 (PEG).

The results from toxicological investigations conducted on Analogue 3 are summarised in the following table. Analogue 3 and the notified chemical are considered to be very similar in chemical composition and therefore the endpoints presented below are likely to reflect the toxicity of the notified chemical.

Details of the provided studies of PEG-8 Beeswax can be found in Appendix A

Endpoint	*Result and Assessment Conclusion*	*Test Substance*
Rat, acute oral toxicity	LD50 > 2000 mg/kg bw;/low toxicity	Analogue 3
Rabbit, skin irritation	slightly irritating	Analogue 3
Rabbit, skin irritation	slightly irritating	Analogue 3 (20%)
Human, skin irritation – Single Patch Test	non-irritating	Analogue 3 (15%)
Rabbit, eye irritation	slightly irritating	Analogue 3
Rabbit, eye irritation	slightly irritating	Analogue 3 (50%)
Rabbit, eye irritation	slightly irritating	Analogue 3 (20%)
Human, skin sensitisation – RIPT	no evidence of sensitisation	Analogue 3 (15%)
Mutagenicity – bacterial reverse mutation	non mutagenic	Analogue 3

Toxicokinetics
Absorption of the notified polymer across biological membranes is likely to be limited, based on the relatively high molecular weight (> 500 Da) and expected low water solubility. However, low molecular weight species are present in the composition of the notified chemical and the possibility of absorption cannot be ruled out. PEG-8 has been shown to be absorbed (50%) by the gastrointestinal tract with most of the chemical subsequently excreted via urine within 24 hours (Fruijtier-Pölloth 2005). PEG-8 does not appear to be metabolised after absorption (CIR 2010). Dermal absorption of analogue 4 has been shown to be dependent on the length of the PEG group (Fruijtier-Pölloth 2005). A study on a small PEG (PEG-4) found that in a worst case scenario (leave-on cosmetic) dermal absorption varied with skin condition (8.42% for intact skin and 33.72% for compromised (tape lifted) skin) (CIR 2010).

Based on the data available for Analogue 4 the notified chemical is not expected to readily penetrate the skin (Fruijtier-Pölloth 2005, CIR 2010).

Acute toxicity.
Analogue 3 was found to be of low acute oral toxicity in a study on rats. Analogues 1 and 4 have also been shown to be of low acute oral toxicity (IJT 1984, Fruijtier-Pölloth 2005, CIR 2010). Based on this the notified chemical is expected to be of low toxicity by the oral route.

Analogue 4, is expected to have low toxicity via the dermal and inhalation routes (Fruijtier-Pölloth 2005, CIR 2010). Analogue 1 was shown to have low dermal toxicity at 2,000 mg/kg, with some animals exhibiting nasal discharge, drooping eyelids, lethargy and diarrhoea (IJT 1984).

Based on this information, the notified chemical is expected to have low acute toxicity through the oral, dermal and inhalation exposure routes.

Irritation and sensitisation.
Analogue 3 was found to be slightly irritating to the skin of rabbits, but not to human skin at a concentration of 15%. Analogue 1 has been shown to be slightly irritating to the skin of animals (IJT 1984). Analogue 4 is expected to have no or slightly irritating effects on the skin of animals and humans (Fruijtier-Pölloth 2005, CIR 2010).

Analogue 3 was found to be slightly irritating to the eye at 20%, 50% and neat concentrations. Analogue 1 was found to be irritating to the eye at a concentration of 13% (IJT 1984) and analogue 4 is expected to have mild, transient eye irritation effects based on studies in rabbits (Fruijtier-Pölloth 2005, CIR 2010).

No evidence of sensitisation on human skin was observed for analogue 3 at a concentration of 15%. Analogue 1 is not expected to exhibit sensitisation effects to human skin (IJT 1984), while analogue 4 is not expected to be a skin sensitiser on healthy skin (Fruijtier-Pölloth 2005, CIR 2010).

Based on this data, the notified chemical is expected to be a slight skin and eye irritant, and is not expected to have the potential for skin sensitisation.

Repeated dose toxicity.
No repeated dose toxicity data were available for analogues 1 or 3. No adverse effects were observed in two subchronic dermal studies conducted on rats and rabbits, using Analogue 1 at a concentration of 13% in two cream formulations (IJT 1984). Analogue 4 is not expected to have strong systemic toxicity (Fruijtier-Pölloth 2005, CIR 2010) or to produce biologically significant embryotoxic or teratogenic effects (CIR 2010). Adverse effects on kidney and liver at very high doses (> 1000 mg/kg bw/day) have been observed for Analogue 4 (Fruijtier-Pölloth 2005). Renal tubular necrosis, renal failure, necrosis of proximal tubules and oxalate crystals have been observed in human burn patients treated with topical ointments containing analogue 4 (CIR 2010). Based on the adverse effects observed in association with severely damaged skin, a risk assessment for kidney effects of PEGs (analogue 4) was conducted by The Personal Care Products Council (PCPC 2009). Based on this assessment, the best available oral no observed effect level (NOEL) for renal toxicity for PEGs of 1,100 mg/kg was determined.

Given this information, together with the expected limited potential for absorption of the notified chemical across biological membranes, the potential for the notified chemical to cause systemic toxicity (particularly adverse renal effects) from repeated exposure is expected to be low.

Mutagenicity/Genotoxicity.
Analogue 3 is not expected to be mutagenic based on a study on bacteria. Analogue 4 is not expected to be mutagenic or genotoxic based on *in vitro* and *in vivo* tests (Fruijtier-Pölloth 2005, CIR 2010).

Based on this information, the notified chemical is not expected to be mutagenic or genotoxic.

Health hazard classification
As no toxicity data were provided, the notified chemical cannot be classified according to the *Globally Harmonised System of 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
Based on the available information, the notified chemical is expected to be of low systemic toxicity, presenting only as a slight skin and eye irritant. The main route of exposure is expected to be dermal with some potential for accidental ocular or oral exposure.

Reformulation
During reformulation workers may be at risk of skin and eye irritation effects when handling the notified chemical at < 100% concentration. This risk should be reduced through the expected use of engineering controls and personal protective equipment (PPE) including eye protection.

Therefore, under the occupational settings described, the risk to the health of workers from use of the notified chemical is not considered to be unreasonable.

End-use
Workers involved in professions where the services provided involve the application of cosmetic products containing the notified chemical to clients (*e.g.* hairdressers and beauty salon workers) may be exposed to the notified chemical. If PPE is used, the risk to these workers 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

Cosmetic products containing the notified chemical at ≤ 12% concentration will be available to the public. The main route of exposure is expected to be dermal with some potential for accidental ocular or oral exposure.

Chemicals such as Analogue 4 have been shown to have increased skin irritation effects and increased potential for dermal absorption where the skin is severely damaged. This issue was addressed by the 2010 CIR Expert Panel (CIR 2010) who found that, based on the available data, a sufficient margin of safety could be maintained between the no observable effect level and the exposure potentially resulting from the use of cosmetic products (leave-on and rinse-off). However, the Panel asserted that the application of cosmetic products containing analogue 4 at high concentrations to skin where the stratum corneum and epidermis were both removed (such as for partial and full thickness burns) would be inappropriate.

Local effects

The notified chemical is expected to be slightly irritating to the skin and eye. Given the low proposed use concentration (≤ 12%) skin irritation effects are not expected. However, the potential for eye irritation effects cannot be excluded.

Systemic effects

No repeat-dose toxicity or metabolism data were available for the notified chemical. However, information was available for the systemic toxicity potential of components of the notified chemical, analogue 1 (beeswax) and analogue 4 (PEG). Analogue 1 has been assessed as safe for use in food with an exposure estimate of 22 mg/kg bw/day determined (EFSA, 2007). A NOEL for renal toxicity of 1,100 mg/kg bw/day was determined by the Personal Care Products Council (PCPC, 2009) for analogue 4.

Based on the estimated NOEL for analogue 4, the repeat dose toxicity potential of the notified chemical was estimated by calculation of the margin of exposure (MoE) of analogue 4 using the worst case exposure scenario from use of multiple products of 3.3408 mg/kg bw/day (see Section 6.1.2). Using a NOEL for renal toxicity of 1,100 mg/kg bw/day, the MoE was estimated to be 329.26. A MoE value ≥ 100 is generally considered to be acceptable for taking into account intra- and inter-species differences.

Therefore, based on the information available, the risk to the public associated with use of the notified chemical at ≤ 12% in 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 in Australia; therefore there is no release of the notified chemical to the environment from this activity. Environmental release during importation, transport and distribution may occur as a result of accidental spills. In the event of a spill, the notified chemical is expected to be contained and collected with an inert absorbent material and disposed of in accordance with local regulations.

The notified chemical will be blended with other ingredients in automated/enclosed facilities to produce cosmetic products. Release from blending is expected to be very low. A total of up to 1 % of the import volume (or up to 10 kg) is estimated to be generated as waste from residues in empty containers during blending. Empty containers containing the notified chemical will either be recycled or disposed of through an approved waste management facility.

RELEASE OF CHEMICAL FROM USE

During use as a component of cosmetic products, the entire volume of the notified chemical in washings is expected to be released to sewers on a nationwide basis. Residues of the notified chemical in the empty containers (up to 3% of the total import volume, or 30 kg) are expected to be disposed of to landfill.

RELEASE OF CHEMICAL FROM DISPOSAL

The majority of the notified chemical is expected to be released to sewer. A small amount of the notified chemical is likely to be disposed of to landfill when empty containers with residues of cosmetic products containing the notified chemical are discarded.

7.1.2. Environmental Fate

No environmental fate studies were submitted for the notified chemical. Following its use in cosmetic products in Australia, the majority of the notified chemical is expected to enter the sewer system before potential release to surface waters nationwide. Based on its chemical structure, the notified chemical is likely to be biodegradable. Notified chemical remaining in treated sewage effluents is likely to be released to surface waters, or applied to land when used for irrigation. Notified chemical in sewage sludge is expected to be disposed of to landfill, or applied to land when sludge is used for soil remediation. Based on its surface activity and expected biodegradability, the notified chemical is not expected to bioaccumulate.

The notified chemical is expected to degrade in STPs, surface waters, soils and landfill due to its expected degradability. The metabolites are expected to further degrade in both the aquatic and terrestrial compartments through biotic and abiotic processes to form water, oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The notified chemical will be released to sewers following its use in cosmetic products. Therefore, under a worst case scenario, it is assumed that 100% of the total import volume of the notified chemical will be discharged into sewers nationwide over 365 days per year. Assuming no removal of the notified chemical in the sewage treatment processes for the worst case scenario, the resultant predicted environmental concentration (PEC) in sewage effluent on a nationwide basis is estimated as follows:

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	200.0	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	0%	
Daily effluent production:	4,523	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.61	µg/L
PEC - Ocean:	0.06	µg/L

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 0.61 µg/L may potentially result in a soil concentration of approximately 4.04 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 20.19 µg/kg and 40.39 µg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity data were submitted. The calculated PEC is well below the EC50 for algae (the most sensitive species) of the most toxic anionic polymers (EC50 > 1 mg/L).

7.2.1. Predicted No-Effect Concentration

A predicted no-effect concentration (PNEC) was not calculated since no ecotoxicity data were available for the notified chemical. Due to its low import volume, low solubility and likelihood for adsorption to sludge and sediment, the notified chemical is not expected to be present in water at concentrations that could be hazardous to aquatic organisms.

7.3. Environmental Risk Assessment

A risk quotient (PEC/PNEC) for the notified chemical was not calculated, as neither a PEC nor PNEC was derived. The notified chemical is unlikely to reach ecotoxicologically significant concentrations in the environment based on its annual importation quantity and use pattern. The notified chemical is not expected to be bioaccumulative based on its high molecular weight. Therefore, based on its annual importation quantity and assessed use pattern the notified chemical, it is not expected to pose an unreasonable risk to the environment.

APPENDIX A: TOXICOLOGICAL INVESTIGATIONS

A.1. Acute toxicity – oral

TEST SUBSTANCE: Analogue 3

METHOD
- Species/Strain: Rat/Sprague-Dawley
- Vehicle: Water
- Remarks - Method: Test substance administered as a 10% (w/v) suspension.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 M, 5 F	2000	0/10

- LD50: > 2000 mg/kg bw
- Signs of Toxicity: None observed.
- Effects in Organs: None observed.
- Remarks - Results: All animals gained the expected amount of body weight. One male (1/5) regurgitated the test substance immediately after exposure. No other clinical signs observed.

CONCLUSION: The notified chemical is of low toxicity via the oral route.

TEST FACILITY: Pharmakon (1995)

A.2. Irritation – skin

TEST SUBSTANCE: Analogue 3(100%)

METHOD
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 3 Male
- Vehicle: None.
- Observation Period: 72 hours
- Type of Dressing: Semi-occlusive.
- Remarks - Method: GLP compliant.
  Test substance was melted in a sheet and applied as a square of 2.5 cm x 2.5 cm (approximately 2 g).

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0	0	0	1	< 24 hours	0
Oedema	0	0	0	0	-	0

* Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.

- Remarks - Results: Very slight erythema was observed in 2/3 animals at the 1 hour observation. No other adverse effects were observed.

CONCLUSION: The test substance is slightly irritating to the skin.

TEST FACILITY: Chrysalis (1997)

A.3. Irritation – skin

TEST SUBSTANCE	Analogue 3 (at 20% concentration)
METHOD	Similar to OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	6 Male
Vehicle	Distilled water
Observation Period	72 hours
Type of Dressing	Occlusive.
Remarks - Method	No significant deviations from protocol described in OECD TG 404. The test substance was exposed to intact skin and abraded skin. Recordings were made at 24 hours and 72 hours.

RESULTS

Lesion	*Mean Score**						*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3	4	5	6			
Intact skin									
Erythema/Eschar	2	1.5	1.5	2	1.5	2	2	-	2
Oedema	0	0	0	0	0	0	0	-	0
Abraded skin									
Erythema/Eschar	2	1.5	1.5	2	1.5	2	2	-	2
Oedema	0.5	0	0	0.5	0	0	1	-	0

* Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animals.

Remarks - Results	No difference in severity of irritation was observed between the effect of the test substance on abraded skin or intact skin in each animal. Well defined erythema was recorded in all animals at the 24 hour observation, with recovery indicated in 3/6 animals at the 72 hour observation. Very slight oedema was recorded in 2/6 animals at the 24 hour observation with recovery indicated in all animals at the 72 hour observation.
CONCLUSION	The test substance (at 20% concentration) is slightly irritating to the skin.
TEST FACILITY	Hazleton (1985)

A.4. Skin irritation – human volunteers

TEST SUBSTANCE	Analogue 3 (at 15% concentration)
METHOD	Single insult patch test
Study Design	Patches containing 0.02 mL test substance (15% w/v) were applied under occlusive dressing for 24 hours. A negative control was performed in parallel. Test sites were examined macroscopically 1 hour after patch removal with cutaneous reactions assessed using a numerical scale similar to that described in OECD TG 404.
Study Group	9 F, 1 M; age range 19 - 41 years
Vehicle	Water
Remarks - Method	Occluded. The test substance was spread on a 0.5 cm × 0.5 cm patch.
RESULTS	
Remarks - Results	All test subjects completed the study. No irritation or adverse effects were observed following exposure to the test substance. The negative control performed as expected.

CONCLUSION	The test substance (at 15% concentration) was non-irritating under the conditions of the test.
TEST FACILITY	IEC (1991)

A.5. Irritation – eye

TEST SUBSTANCE	Analogue 3 (neat)
METHOD	Similar to OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	6 Male
Observation Period	7 days
Remarks - Method	There were no significant deviations from the protocol described in OECD TG 405. No topical anaesthetics or systemic analgesics were used. No initial test was performed. Recordings were made at 1 hour, 1, 2, 3, 4 and 7 days following exposure.

RESULTS

Lesion	*Mean Score**						*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3	4	5	6			
Conjunctiva: redness	0	0	0	0	0	0.6	2	72 hours	0
Conjunctiva: chemosis	0	0.3	0.3	0.6	0	0	2	72 hours	0
Conjunctiva: discharge	0	0	0	0	0	0	1	24 hours	0
Corneal opacity	0	0	0	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	0	0	1	24 hours	0

* Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animals.

Remarks - Results	Conjunctival swelling (slight to obvious), redness and discharge and iridial inflammation were observed in all animals 1 hour after exposure to the test substance. Recovery from conjunctival effects was observed at 24 (slight swelling in 3/6 animals, slight redness in 1/6 animals) and 48 hours (slight swelling in 1/6 animals, slight redness in 1/6 animals) with recovery in all animals 72 hours following exposure. No iridial inflammation was observed 24 hours after exposure. No corneal effects were recorded following exposure to the test substance.
CONCLUSION	The test substance is slightly irritating to the eye.
TEST FACILITY	IFREB (1982)

A.6. Irritation – eye

TEST SUBSTANCE	Analogue 3 (at 50% concentration)
METHOD	Similar to OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	6 Male
Observation Period	7 days
Remarks - Method	The test substance was diluted to 50% w/v in distilled water. There were no significant deviations from the protocol described in OECD TG 405. No topical anaesthetics or systemic analgesics were used. No initial test was performed. Recordings were made at 1 hour, 1, 2, 3, 4 and 7 days following exposure.

RESULTS

Lesion	*Mean Score**						*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3	4	5	6			
Conjunctiva: redness	0.3	0.3	0.3	0.6	1	0.3	3	72 hours	0
Conjunctiva: chemosis	0.3	0	0	0	0	0	1	48 hours	0
Conjunctiva: discharge	0	0	0	0	0	0	2	24 hours	0
Corneal opacity	0	0	0	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	0	0	0	-	0

* Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animals.

Remarks - Results

Mild to severe conjunctival redness (1/6 animals mild, 4/6 animals moderate, 1/6 animals severe) and discharge (2/6 animals mild, 3/6 animals moderate, 1/6 animals severe) was observed in all animals 1 hour after exposure. Slight conjunctival swelling was observed in all animals.

Recovery from conjunctival effects was observed at 24 (slight swelling in 1/6 animals, slight redness in 5/6 animals, moderate redness in 1/6 animals) and 48 hours (slight redness in 2/6 animals) with recovery in all animals 72 hours following exposure.

No iridial inflammation or corneal effects were recorded following exposure to the test substance.

CONCLUSION

The test substance (at 50% concentration) is slightly irritating to the eye.

TEST FACILITY

EviC-CEBA (1982)

A.7. Irritation – eye

TEST SUBSTANCE

Analogue 3 (20% concentration)

METHOD

Similar to OECD TG 405 Acute Eye Irritation/Corrosion.

Species/Strain: Rabbit/New Zealand White

Number of Animals: 6 Male

Observation Period: 7 days

Remarks - Method: The test substance was diluted to 20% w/v in distilled water. There were no significant deviations from the protocol described in OECD TG 405. No topical anaesthetics or systemic analgesics were used. No initial test was performed.
Recordings were made at 1 hour, 1, 2, 3, 4 and 7 days following exposure.

RESULTS

Lesion	*Mean Score**						*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3	4	5	6			
Conjunctiva: redness	0	0.6	0.6	0	0.3	0.3	2	72 hours	0
Conjunctiva: chemosis	0.3	0.6	0.3	0.3	0.3	0.3	2	72 hours	0
Conjunctiva: discharge	0	0	0	0	0	0	1	24 hours	0
Corneal opacity	0	0	0	0.3	0	0	1	48 hours	0
Iridial inflammation	0	0	0	0	0	0	0	-	0

* Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animals.

Remarks - Results	Slight to mild conjunctival swelling (5/6 and 1/6 animals respectively), mild discharge (4/6 animals) and slight to mild redness (5/6 and 1/6 animals respectively) were observed 1 hour after exposure. Circumcorneal injections were also observed in all animals. No iridial inflammation was observed. Recovery from conjunctival effects was observed at 24 (slight swelling in all animals, slight redness in 4/6 animals) and 48 hours (slight swelling in 1/6 animals, slight redness in 2/6 animals) with recovery in all animals 72 hours following exposure. Circumcorneal injections persisted in 1/6 animals, with recovery observed at the 48 hour observation. Marked iridial inflammation was observed in 1/6 animals at the 24 hour observation, with full recovery observed at the 48 hour observation. Full recovery in all animals was observed at the 72 hour observations.
CONCLUSION	The test substance (at 20% concentration) is slightly irritating to the eye.
TEST FACILITY	Hazleton (1985)

A.8. Skin sensitisation – human volunteers

TEST SUBSTANCE	Analogue 3
METHOD	Repeated insult patch test with challenge
Study Design	Induction Procedure: Patches containing 0.02 mL test substance (15% v/v) were applied 3 times per week (Monday, Wednesday and Friday) for a total of 9 applications. Patches were removed after 48 h (or 72 h for patches applied on Friday) and graded . Rest Period: 15 days Challenge Procedure: A patch was applied to a naïve site. Patches were removed after 48 h. Sites were graded 24 and 48 h post-patch removal.
Study Group	20 F, 5 M; age range 20 - 56 years
Vehicle	Distilled water.
Remarks - Method	Occluded. The test substance was spread on a circular patch of filter paper, 7 mm in diameter (0.4 cm^2). Test conducted according to the Marzulli and Maibach method.
RESULTS	
Remarks - Results	24/25 subjects completed the study. One subject withdrew for reasons unrelated to the treatment (4 induction observations recorded). Slight erythema was observed for 5 and 3 subjects at the first and final induction observations respectively. Two subjects exhibited worn skin (1 subject at the final induction observation and 1 subject at the first challenge observation). No adverse responses were noted at challenge.
CONCLUSION	The test substance (at 15% concentration) was non-sensitising under the conditions of the test.
TEST FACILITY	IEC (1995)

A.9. Genotoxicity – bacteria

TEST SUBSTANCE	Analogue 3
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. Plate incorporation procedure

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, TA102
Metabolic Activation System	Aroclor 1254 induced rat liver S9 mix
Concentration Range in Test 1	a) With metabolic activation: 52, 164, 512, 1,600 and 5,000 µg/plate b) Without metabolic activation: 52, 164, 512, 1,600 and 5,000 µg/plate
Concentration Range in Test 2	a) With metabolic activation: 492, 878, 1,568, 2,800 and 5,000 µg/plate b) Without metabolic activation: 492, 878, 1,568, 2,800 and 5,000 µg/plate
Vehicle	Water
Remarks - Method	GLP compliant. No significant protocol deviation. A dose-selection pre-test (concentration range of 52 – 5000 µg/plate, tested in the presence and absence of metabolic activation) was performed on TA100 and these results acted as the results for this strain in Test 1 of the main test. Positive controls: without metabolic activation – 2-Nitrofluorene (TA98), sodium azide (TA100, TA1535), 9-Aminoacridine (TA1537), t-BHP (TA102); with metabolic activation – 2-aminoanthracene.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 5,000 µg	> 5,000 µg	> 5,000 µg	negative
Test 2		> 5,000 µg	> 5,000 µg	negative
Present				
Test 1	> 5,000 µg	> 5,000 µg	> 5,000 µg	negative
Test 2		> 5,000 µg	> 5,000 µg	negative

Remarks - Results	Under the conditions of test 1, a statistically significant increase in the number of revertants was observed for strain TA1537 at 512 µg/plate in the absence of metabolic activation, and strain TA102 at 512 µg/plate to 5,000 µg/plate in the presence of metabolic activation. A dose-response relationship was observed with the number of revertants in strain TA102 (presence of metabolic activation). However, these increases in revertants were not considered biologically relevant by the study authors as the changes were small and not reproducible. Under the conditions of test 2, no significant increases in the frequency of revertant colonies were observed for any of the bacterial strains, with any dose of the test substance, either with or without metabolic activation. The positive and negative controls gave a satisfactory response confirming the validity of the test system.
CONCLUSION	The test substance was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Pharmakon (1996)

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