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December 2015

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

L-Isoleucine, C_{12-22}-alkyl esters, ethanesulfonates (INCI name: Brassicyl Isoleucinate Esylate)

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.

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
STD/1569	A.S. Harrison & Co Pty Limited	L-Isoleucine, C_{12-22}-alkyl esters, ethanesulfonates (INCI name: Brassicyl Isoleucinate Esylate)	ND*	≤ 10 tonnes per annum	Cosmetic ingredient

*ND= Not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on limited toxicity data, 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).

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.

Based on the available information, when used at 1.5% in body lotions and hand cream, 5% in hair styling products, shampoo, hair conditioner and hairspray, and 1% in other 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 reported 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 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 or accidental release of the notified chemical should be handled by containment, physical 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 concentration of the notified chemical exceeds or is intended to exceed 1.5% in body lotions and hand cream, 5% in hair styling products, shampoo, hair conditioner and hairspray, and 1% in other rinse-off cosmetic products;
- additional information becomes available on the repeat 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 ingredient in cosmetics, 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 mixture containing the notified chemical provided by the notifier was 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

This notification has been conducted under the cooperative arrangement with Canada. The health and environmental hazard assessment components of the Canadian report were provided to NICNAS and, where appropriate, used in this assessment report. The other elements of the risk assessment and recommendations on safe use of the notified chemical were carried out by NICNAS.

APPLICANT
A. S. Harrison & Co Pty Ltd (ABN: 89 000 030 437)
75 Old Pittwater Rd
BROOKVALE NSW 2100

NOTIFICATION CATEGORY
Standard (Reduced fee notification): Chemical other than polymer (more than 1 tonne 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 hydrolysis as a function of pH, partition coefficient, adsorption/desorption and water solubility

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Canada (2013)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Emulsense (containing the notified chemical at ≤ 65% concentration)

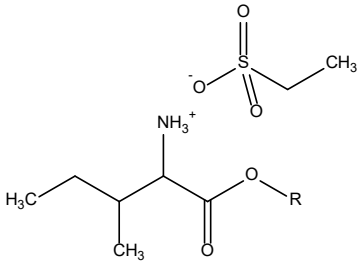
CAS NUMBER
1156505-34-8

CHEMICAL NAME
L-Isoleucine, C_{12-22}-alkyl esters, ethanesulfonates

OTHER NAME(S)
Brassicyl Isoleucinate Esylate (INCI name)
Emulsense HC (containing the notified chemical at ≤ 25% concentration)
Emulsense SC (containing the notified chemical at ≤ 25% concentration)

MOLECULAR FORMULA
Unspecified

STRUCTURAL FORMULA



where R = C12 - C22 linear, saturated and on average R = 21

MOLECULAR WEIGHT
408-548 Da
534 Da (R = 21)

ANALYTICAL DATA
Reference IR spectra was provided for the mixture containing the notified chemical at ~ 65% concentration.

3. COMPOSITION

DEGREE OF PURITY
≤ 65%*

*The notified chemical is manufactured as a reaction product of isoleucine, ethanesulfonic acid and Brassica alcohol (CAS No. 661-19-8, 112-92-5). A large quantity of Brassica alcohol (≤ 35%) remains unreacted in the final product, Emulsense. Emulsense (containing the notified chemical at ≤ 65% concentration) is blended with other compounds (Brassica glycerides, Brassica alcohol) to manufacture Emulsense HC and Emulsense SC containing the notified chemical at ≤ 25% concentration.

4. PHYSICAL AND CHEMICAL PROPERTIES
The following physico-chemical properties are for a mixture of 65% notified chemical and 35% unreacted Brassica alcohol.

APPEARANCE AT 20 °C AND 101.3 kPa: yellow coloured flakes

Property	Value	Data Source/Justification
Melting Point	57.3 °C	Measured
Boiling Point	> 300 °C at 101.3 kPa	Calculated (EpiSuite, MPBWIN v.1.43)
Density	887.2 kg/m^3 at 100 °C	Measured
Vapour Pressure	< 10^{-8} kPa at 25 °C	Calculated (EpiSuite, MPBWIN v.1.43)
Water Solubility	Immiscible in cold water, sparingly soluble at high temperature	SDS
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionalities; however, not expected to hydrolyse based on low water solubility
Partition Coefficient (n-octanol/water)	Not determined	Expected to partition to phase boundaries based on surfactant properties
Adsorption/Desorption	Not determined	Expected to adsorb strongly to soil and sediment based on surfactant properties
Dissociation Constant	Not determined	The notified chemical is a salt and is expected to be ionised under environmental conditions (pH 4-9)
Flash Point	> 198 °C	Measured
Flammability	Not determined	Not expected to be flammable based on flash point
Autoignition Temperature	Predicted negative	Based on chemical structure
Explosive Properties	Predicted negative	Based on chemical structure
Oxidising Properties	Predicted negative	Based on chemical structure

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 within Australia. The notified chemical will be imported either as a component of finished cosmetic products (at ≤ 5% concentration), or as a component of a mixture (at ≤ 65% concentration) for reformulation of cosmetic products.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	1-10	1-10	1-10	1-10	1-10

PORT OF ENTRY
Sydney and Melbourne

TRANSPORTATION AND PACKAGING
The notified chemical will be imported as a component of a mixture (at ≤ 65% concentration) in ~ 23 kg steel drums by ship. The imported mixture containing the notified chemical will be transported to reformulation sites by road. The formulated products will be packaged in containers suitable for retail sale. The notified chemical will also be imported to Australia as a component of finished products (at ≤ 5% concentration) in consumer packaging (in bulk cartons) by ship. The imported finished products will be transported to distributor's sites by road.

USE
The notified chemical will be used as an ingredient in cosmetic products at ≤ 5% concentration. The content in the final consumer products will vary, with the following proposed usage concentrations: body lotions and hand cream (≤ 1.5%); hair styling products, shampoo, hair conditioner and hairspray (≤ 5%); and other rinse-off cosmetic products (≤ 1%).

OPERATION DESCRIPTION
The notified chemical will be imported either as a component of finished cosmetic products (at ≤ 5% concentration), or as a component of a mixture (at ≤ 65% concentration) for reformulation of cosmetic products.

Reformulation
When reformulated, the mixture containing the notified chemical (at ≤ 65% concentration) will be blended into cosmetic products at customer sites. Procedures will vary depending on the nature of the cosmetic product being formulated, and may involve both automated and manual transfer steps. However, in general, it is expected that the reformulation processes will involve blending operations that will be highly automated and occur in enclosed environments, followed by automated filling of the reformulated products into containers of various sizes.

End-use
The finished cosmetic products containing the notified chemical at ≤ 5% concentration will be used by consumers and professionals (such as beauticians and hair dressers). Depending on the nature of the products, application 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)*
Transport and storage	1-2	20-30
Reformulation	1-3	30
Retail workers	> 8	240
Professionals	> 8	240

EXPOSURE DETAILS

Transport and storage

Transport and storage workers may come into contact with the notified chemical (at ≤ 65% concentration) only in the unlikely event of an accidental rupture of containers.

Reformulation

During reformulation into cosmetic products, dermal, ocular and inhalation exposure of workers to the notified chemical at ≤ 65% concentration may occur during weighing and transfer stages, blending, quality control analysis, and cleaning and maintenance of equipment. Exposure is expected to be minimised through the use of local and general ventilation and/or enclosed systems, and through the use of personal protective equipment (PPE) such as coveralls, safety glasses, and impervious gloves.

End-use

Exposure to the notified chemical in end-use products (at ≤ 5% concentration) may occur in professions where the services provided involve the application of cosmetic products to clients (i.e., hair and beauty salons). 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 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 a wide range of cosmetic products. The principal route of exposure will be dermal, while ocular and inhalation exposure (e.g. through the use of spray products) are also possible.

Data on typical use patterns of cosmetic products containing the notified chemical may be used are shown in the following tables (SCCS, 2012; Cadby *et al.,* 2002; 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 100% was assumed for the notified chemical (ECHA, 2014). 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%, which accounts for a number of other exposure considerations (e.g., the amount ending up on the hair, as intended). A lifetime average female body weight (BW) of 64 kg (enHealth, 2012) was used for calculation purposes.

- Cosmetic products (Dermal exposure):

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (mg/kg bw/day)
Body lotion	7820	1.5	1	1.8328
Hand cream	2160	1.5	1	0.5063
Hair styling products	4000	5	0.1	0.3125
Shower gel	18670	1	0.01	0.0292
Hand wash soap	20000	1	0.01	0.0313
Shampoo	10460	5	0.01	0.0817
Hair conditioner	3920	5	0.01	0.0306
Facial cleanser	800	1	0.01	0.0013
Total				2.8256

C = concentration of notified chemical
RF = retention factor (unit less)
Daily systemic exposure = (Amount x C x RF x DA)/BW

-Cosmetic products (hair spray)

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	5	20	1	20	50	1	10	0.1610

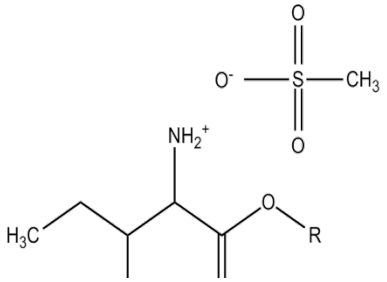
C = concentration of notified chemical
Daily systemic exposure = [(Amount x C x Inhalation Rate x Fraction Inhaled x 0.1)/(body weight x 1440)] x [(Exposure Duration (Zone 1)/Volume (Zone 1)) + (Exposure Duration (Zone 2)/Volume (Zone 2))]

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 2.9866 mg/kg bw/day for the notified chemical. It is acknowledged that inhalation exposure to the notified chemical from use of other cosmetic products (in addition to hair spray) 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 100% 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

The results from toxicological investigations conducted on a mixture of 65% notified chemical and 35% unreacted Brassica alcohol, and suitable analogues are summarised in the table below.

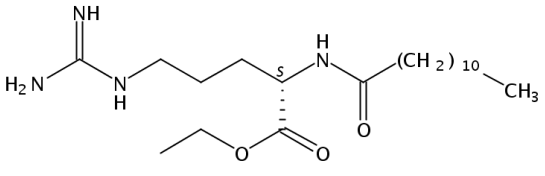
Analogue 1
Chemical name: L-Isoleucine, C_{12-22}-alkyl esters, ethanesulfonates
CAS number: 1156505-34-8



R = C12-C22 (predominantly 20)

Analogue 1 is structurally similar to the notified chemical with only minor differences, and is therefore considered acceptable to estimate the acute oral toxicity of the notified chemical.

Analogue 2
Chemical name: L-Arginine, N^2-(1-oxododecyl)-, ethyl ester, hydrochloride (1:1)
CAS number: 60372-77-2



- HCl

Like the notified chemical analogue 2 is a cationic surfactant comprised of a primary ammonium cation and a long alkyl chain. Analogue 2 is also of similar molecular weight. Although the counterion for analogue 2 differs from that of the notified chemical, the nature of the counterion is not expected to have a significant contribution

to the hazardous properties of the chemical. Analogue 2 is therefore considered acceptable as a reasonable estimation of the sensitisation, repeat dose toxicity and genotoxicity potential for the notified chemical.

Endpoint	*Test substance*	*Result and Assessment Conclusion*
Rat, acute oral toxicity	Analogue 1	LD50 > 2,000 mg/kg bw; low toxicity
Skin irritation (in vitro) (EpiDerm assay)	Notified chemical*	non-irritating
Eye irritation (in vitro) (EpiOcular Assay)	Notified chemical*	non-irritating
Eye irritation (in vitro) (HET-CAM Assay)	Notified chemical*	none to slightly irritating
Human, skin sensitisation – RIPT (10%)	Notified chemical*	no evidence of sensitisation at 6.5% concentration
Guinea pig, skin sensitisation – Magnusson and Kligman test	Analogue 2	no evidence of sensitisation at up to 20% concentration
Rat, repeat dose toxicity, diet – 90 days.	Analogue 2	NOAEL 346 mg/kg bw/day
Rat, repeat dose toxicity, diet – 52 weeks	Analogue 2	NOAEL 271 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	Notified chemical*	non-mutagenic
Genotoxicity – in vitro mammalian chromosome aberration test	Analogue 2	non-genotoxic
Genotoxicity – in vitro mammalian cell mutation test	Analogue 2	non-genotoxic

*Test substance was a mixture of 65% notified chemical and 35% unreacted Brassica alcohol

Toxicokinetics.
Toxicokinetic data on the notified chemical was not provided. The moderately high molecular weight (> 500 Da) and ionic character of the notified chemical suggests that absorption across biological membranes would be limited.

Acute toxicity.
No acute oral, dermal or inhalation toxicity data were provided for the notified chemical. An acute oral toxicity study with analogue 1 gave an LD50 value of > 2000 mg/kg bw indicating low acute oral toxicity for the notified chemical (Canadian report). The notified chemical is also expected to be of low acute dermal toxicity based on the limited potential for dermal absorption.

Irritation and sensitisation.
The mixture containing the notified chemical at 65% concentration was found to be non-irritating to skin and eyes in an EpiDerm and EpiOcular MTT Viability assay, respectively (Canada report). The mixture containing the notified chemical at 65% concentration was also found not to give an irritation response in a HET-CAM test. Based on the classification interpretation for the test, the result corresponds to a classification of none to slight eye irritation potential (Canadian report). The notified chemical is therefore expected to have a low potential for skin and eye irritation.

A 10% aqueous solution of a mixture containing the notified chemical at 65% concentration (equivalent to 6.5% notified chemical) did not show any evidence of sensitisation in a human repeat insult patch test (HRIPT) using 56 subjects only (Canadian report). No other dermal sensitisation study was provided for the notified chemical. The notified chemical and its metabolites have no protein binding alerts (OECD Toolbox v.3.2), and bioavailability of the notified chemical is expected to be low.

Two dermal sensitisation studies (Magnusson and Kligman test, OECD 406) were performed on analogue 2 (SCCP, 2007). The results indicate that analogue 2 does not induce a sensitisation response in the guinea pig at 18% (first study) and 20.4% (second study) concentration (SCCP, 2007).

Overall, based on the weight of evidence, the notified chemical is expected to have a low potential for sensitisation.

Repeated dose toxicity.
There was no repeated dose toxicity data on the notified chemical.

Two repeated dose toxicity studies are available for analogue 2 (SCCP, 2007).

In a subchronic 13 week study, rats (20/sex/dose) were fed with analogue 2 incorporated in the diet at final doses of 5000, 15,000 and 50,000 ppm. Group mean dosages over the treatment period were 346, 1030 and 3346 mg/kg bw/day for males and 401, 1159 and 3527 mg/kg bw/day for females. The main treatment-related pathological changes observed were in the non-glandular region of the stomach, specifically in the area adjacent to the entry of the oesophagus. The predominant change was parakeratosis, present in the majority of the high dose males and females and in one mid dose female. Ulceration was seen in 1 high dose and 1 mid dose male and two high dose females. In addition, erosions and epithelial hyperplasia were seen in all the high dose females. This was considered to indicate that the test substance had an irritant action on mucosal tissue, but that it was unusual for the changes to be restricted to such a specific area, e.g. adjacent to the entry of the oesophagus. The No Observed Adverse Effect Level (NOAEL) was considered to be 346 mg/kg bw/day for males and 401 mg/kg bw/day for females.

In the chronic 52 week study, rats (20/sex/dose) were fed with analogue 2 incorporated into the diet. Overall group mean achieved intakes at 2000, 6000 and 18,000 ppm for the treatment period were 93.5, 271 and 800 mg/kg bw/day for males and 131, 393 and 1128 mg/kg bw/day for females. Low bodyweight gain and initial reduced food consumption in both sexes were noted at the 6000 and 18000 ppm dosage levels. These bodyweight changes at both 6000 and 18,000 ppm were considered to be treatment-related, but at 6000 ppm, based on a combination of the short duration, the magnitude of difference from controls, lack of adverse effects on survival or general condition of the animals, they were not considered to be of toxicological importance. Animals receiving 18,000 ppm showed a more pronounced effect on bodyweight gain and irritant effects of treatment on the forestomach with limited ulceration and signs of healing. The study authors considered the observed white cell disturbances were not of toxicological importance, since there was no clear dose-relationship. In support of this, there were no treatment related effects on the bone marrow and a lack of any histopathology findings associated with the lymphoid tissues. The study authors concluded that no significant toxicological effects were observed in the animals receiving 6000 ppm or 2000 ppm of analogue 2 in the diet. The No Observed Adverse Effect Level (NOAEL) was considered to be 271 mg/kg bw/day for males and 393 mg/kg bw/day for females.

In the absence of adequate data on the chronic toxicity of the notified chemical, data on analogue 2 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 271 mg/kg bw/day.

Mutagenicity/Genotoxicity.
The mixture containing the notified chemical at 65% concentration was found to be non-mutagenic in a bacterial reverse mutation assay (Canadian report). No further genotoxicity studies were provided for the notified chemical.

Analogue 2 was found to be non-mutagenic in two *in vitro* mammalian cell mutation assays (at 20.3% and 88.2% concentration, respectively) and one *in vitro* mammalian chromosome aberration test (at 93.3% concentration) (SCCP, 2007).

Based on the available information, the notified chemical is not expected to be genotoxic.

Health hazard classification
Based on limited toxicity data, 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
Reformulation
Workers may experience dermal, ocular and inhalation exposure to the notified chemical (at ≤ 65% concentration) during reformulation. The use of enclosed, automated processes and PPE (i.e., coveralls, goggles, and impervious gloves) should minimise the potential for exposure. Based on the expected control measures in place to minimise worker exposure and the overall low toxicity of the notified chemical, the risk to workers from use of the notified chemical is not considered to be unreasonable.

End use
Hair and beauty care professionals will handle the notified chemical at ≤ 5% concentration when applying products containing it to clients. Such professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified chemical (for details of the public health risk assessment, see Section 6.3.2).

6.3.2. Public Health
The general public will be repeatedly exposed to the notified chemical during use of cosmetic products containing the notified chemical at ≤ 5% concentration.

Repeated dose toxicity
The potential systemic exposure to the public from the use of the notified chemical in cosmetic products was estimated to be 2.9866 mg/kg bw/day. Using a NOAEL of 271 mg/kg bw/day, which was derived from a chronic study on analogue 2, the Margin of Exposure (MoE) was estimated to be 91. A MoE value greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences. However, it is acknowledged that the calculations are conservative, given the assumption of 100% dermal absorption for the notified chemical. Furthermore, the assumption that an adult consumer will use daily a large number of cosmetics containing the notified chemical at up to 5% concentration, is conservative, and likely to overestimate exposure under realistic use scenarios. Therefore, the MoE is considered to be acceptable.

As the notified chemical may have the potential to enhance dermal absorption of other chemicals due to its surfactant activity, care should be taken in formulating end-use products containing it.

Based on the available information, the risk to the public associated with the use of the notified chemical at ≤ 5% 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 be imported as a component of raw material for reformulation into finished cosmetic products, or as a component of finished cosmetic formulations. There is unlikely to be any significant release to the environment from transport and storage, except in the case of accidental spills and leaks. In the event of spills, the product containing the notified chemical is expected to be collected with inert material, and disposed of to landfill in accordance with local government regulations.

The reformulation process will involve manual transfer of the raw material containing the notified chemical into blending vessels, followed by blending operations that are expected to be highly automated and occur within a fully enclosed environment. Therefore, significant release of the notified chemical from this process to the environment is not expected. The process will be followed by automated filling of the formulated products into end-use containers of various sizes. Wastes containing the notified chemical generated during reformulation include equipment wash water, spilt materials, and empty import containers. Wastes may be collected and released to sewers, or disposed of to landfill in accordance with local government regulations.

RELEASE OF CHEMICAL FROM USE
The majority of the notified chemical is expected to be released to sewer across Australia as a result of its use in various cosmetic formulations, which will be washed off the hair and skin of consumers and disposed of to the sewer. A small proportion of the notified chemical is expected to be disposed of to landfill as residue in empty end-use containers.

RELEASE OF CHEMICAL FROM DISPOSAL
A small proportion of the notified chemical may remain in end-use containers once the consumer products are used up. Wastes and residues of the notified chemical in empty containers are likely either to share the fate of the container and be disposed of to landfill, or to be released to sewer when containers are rinsed before recycling through an approved waste management facility.

7.1.2. Environmental Fate

Following its use in cosmetic formulations, the majority of the notified chemical is expected to enter the sewer system, before potential release to surface waters nationwide. Based on the results of a biodegradability study (carried out in accordance with OECD 301 B test guidelines), the notified chemical is considered to be readily biodegradable (78.08% in 28 days). Based on its low water solubility and cationic properties, the notified chemical is expected to bind strongly to sludge and sediment. The notified chemical is expected to partition to phase boundaries based on its surfactant properties, and along with its ready biodegradability, is therefore not expected to be bioaccumulative. In surface waters, the notified chemical is expected to adsorb to soil and sediment, and eventually degrade through biotic and abiotic processes to form water and oxides of carbon and nitrogen.

The majority of the notified chemical will be released to sewer after use. A proportion of the notified chemical may be applied to land when effluent is used for irrigation, or when sewage sludge is used for soil remediation, or disposed of to landfill as collected spills and empty container residue. The notified chemical residues in landfill, soil and sludge are expected to eventually degrade to form water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated to assume a worst case scenario, with 100% release of the notified chemical into sewer systems nationwide and no removal within sewage treatment plants (STPs).

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	10,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	10,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	27.40	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:	6.058	µg/L
PEC - Ocean:	0.606	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 6.058 µg/L may potentially result in a soil concentration of approximately 40.39 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of the notified chemical in the applied soil in 5 and 10 years may be approximately 201.9 µg/kg and 403.9 µg/kg, respectively.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h LL50 > 65 mg/L (WAF*)	Not harmful to fish up to water solubility limit
Daphnia Toxicity	48 h EL50 > 65 mg/L (WAF*)	Not harmful to *Daphnia* up to water solubility limit
Algal Toxicity	72 h E_rL50 > 65 mg/L (WAF*)	Not harmful to algae up to water solubility limit

* Water Accommodated Fraction

Based on the ecotoxicological endpoints for the notified chemical, it is not expected to be harmful to aquatic life up to the limit of its solubility in water. Therefore, the notified chemical is not formally classified under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009) for acute and chronic toxicities.

7.2.1. Predicted No-Effect Concentration

The predicted no-effects concentration (PNEC) has been calculated from the most sensitive ecotoxicological endpoint. A safety factor of 100 was used given acute endpoints for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LL50 (Fish, 96 h)	> 65	mg/L
Assessment Factor	100	
Mitigation Factor	1.00	
PNEC:	> 650	µg/L

7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) has been calculated based on the predicted PEC and PNEC.

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	6.058	> 650	**< 0.009**
Q - Ocean	0.606	> 650	**< 0.001**

The risk quotient for discharge of treated effluents containing the notified chemical to the aquatic environment indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in surface waters, based on its maximum annual importation quantity. The notified chemical is readily biodegradable, and is expected to have a low potential for bioaccumulation. On the basis of the PEC/PNEC ratio, maximum annual importation volume and assessed use pattern in cosmetic formulations, the notified chemical is not expected to pose an unreasonable risk to the environment.

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