File No: LTD/1780

January 2015

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Isooctadecanoic acid, hydrogenated castor-oil alkyl esters

(INCI name: Hydrogenated Castor Oil Isostearate)

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

TABLE OF CONTENTS

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/1780	L'Oreal Australia Pty Ltd	Isooctadecanoic acid, hydrogenated castor-oil alkyl esters (INCI name: Hydrogenated Castor Oil Isostearate)	ND*	≤ 1 tonne per annum	Cosmetic ingredient

ND*: Not Determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical is not 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.

Based on the available information, when used at ≤ 10% in body lotions and ≤ 15% in other cosmetic products (excluding products to be applied by aerosol spray), the notified chemical is not considered to pose an unreasonable risk to public health.

Environmental risk assessment
Based on 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

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical during reformulation processes:
  - Enclosed, automated processes, where possible

- 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, safety glasses

  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.

Disposal

- Where reuse or recycling are not available or 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, 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;
- if the notified chemical is intended to be used in products to be applied by aerosol spray;

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 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 the product containing it were provided by the notifier and 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)
L'Oreal Australia Pty Ltd (ABN: 40 004 191 673)
564 St Kilda Rd
Melbourne VIC 3004

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: other names, molecular and structural formulae, molecular weight, analytical data, degree of purity, impurities, additives/adjuvants and use details.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: density, vapour pressure, hydrolysis as a function of pH, adsorption/desorption, dissociation constant, flash point, autoignition temperature, explosive properties and oxidising properties.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None.

NOTIFICATION IN OTHER COUNTRIES
EU (France, 2005)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Hydrogenated Castor Oil Isostearate (INCI Name)

CAS NUMBER
533910-01-9

CHEMICAL NAME
Isooctadecanoic acid, hydrogenated castor-oil alkyl esters

MOLECULAR WEIGHT
> 350 Da

ANALYTICAL DATA
Reference NMR, IR, UV/VIS and HPLC spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 95%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: White to pale yellow paste.

Property	Value	Data Source/Justification
Freezing Point	-20.5 to -20.9 °C	Measured
Boiling Point	No boiling point up to 400 °C (decomposed before boiling)	Measured
Density	Not determined	-
Vapour Pressure	Not determined	Expected to be low.
Water Solubility	8.9×10^{-3} g/L at 20 °C	Measured
Hydrolysis as a Function of	Not determined	Contains hydrolysable functionalities.

pH		However, the notified chemical is not expected to significantly hydrolyse under the normal environmental pH range of 4-9
Partition Coefficient (n-octanol/water)	log Pow = 12.4 - 29.7	Calculated. KOWIN v1.68, EPI Suite v4.1 (US EPA, 2010)
Adsorption/Desorption	log K_{oc} = 18.2 (MCI method) log K_{oc} = 16.8 (Kow method)	Calculated. KOCWIN v2.0, EPI Suite v4.1 (US EPA, 2010)
Dissociation Constant	Not determined	Contains dissociable functionality. Therefore, the notified chemical has potential to dissociate under normal environmental conditions (pH 4 – 9).
Flash Point	287 °C	(M)SDS
Flammability	Not "highly flammable"	Measured
Autoignition Temperature	Not determined	Not expected to autoignite under normal conditions of use.
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties.
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties.

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 as a neat chemical for reformulation and/or as a component of end-use cosmetic products.

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 or Melbourne.

TRANSPORTATION AND PACKAGING
The notified chemical in its neat form will be imported in 16 kg drums on pallets. Products containing the notified chemical will be packed in bottles and tubes (sizes up to 500 mL; made mainly from HDPE) inside shippers, with multiple shippers per pallet and multiple pallets per shipping container. Within Australia, the products will be transported by road and/or rail.

USE
The notified chemical will be used as a cosmetic ingredient in a variety of products (at proposed usage concentrations of ≤ 10% in body lotions, ≤ 5% in aerosol spray products and ≤ 15% in other cosmetic products).

OPERATION DESCRIPTION
Reformulation
When reformulated in Australia, the notified chemical will be blended into end-use consumer products at customer sites. Procedures will vary depending on the nature of the cosmetic product being formulated. Both manual and automated steps will be involved. For example, manual processes could include weighing of an appropriate amount of the notified chemical into a container then adding the chemical directly into a mixing

tank, with periodic sampling for quality control purposes carried out during the manufacturing process. Automated processes may include mixing stages and filling of end-use containers with products.

End-use
Finished products containing the notified chemical (≤ 15% concentration) may be used by consumers and professionals, such as hairdressers and workers in beauty salons. Depending on the nature of the product, the application could be by hand or using 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
Professional compounder	8	12
Chemist	3	12
Packers	8	12
End users (workers)	8	365

EXPOSURE DETAILS
Transport and storage
Transport and storage workers may come in contact with the notified chemical either in neat form or at various concentrations in cosmetic products (≤ 15%), only in the event of accidental rupture of containers.

At the notifier facility, the primary work activity undertaken by transport and warehouse workers will include the handling, loading and off-loading of drums containing the notified chemical at ≤ 100% concentration. Exposure of these workers will be limited to situations involving products sampling for quality control or, in the event of a discharge, clean up from a spill or leaking drum. If such an event occurs, a worker may be exposed through dermal or ocular contact. The notifier has indicated that such exposures will be minimised to the extent possible through the use of personal protective equipment (PPE).

Reformulation
During reformulation into cosmetic products, dermal and ocular exposure of workers may occur when handling the notified chemical or products containing it. Exposure is expected to be minimised through the use of exhaust ventilation and/or automated/enclosed systems as well as through the use of PPE, such as coveralls, safety glasses and impervious gloves.

End-use
Exposure to the notified chemical in end-use products (at ≤ 15% concentration) may occur in professions where the services provided involve the application of cosmetic products to clients (e.g. hair dressers, workers in beauty salons). The principal route of exposure will be dermal, while ocular and inhalation 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 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 through the use of the cosmetic products (≤ 15% concentration in individual products). The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray.

A combined internal dose of 5.243 mg/kg bw/day was estimated using data on typical use patterns of cosmetic products in which the notified chemical may be used (SCCS, 2012; SDA, 2005; specific use details of the notified chemical are considered as exempt information). This estimation assumed a worst case scenario and is for a person who is a simultaneous user of a selection of cosmetic products that may contain the notified chemical.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the following table. For full details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days.	NOAEL = 1,000 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mouse lymphoma cells	non genotoxic
Rat, developmental toxicity	NOAEL = 300 mg/kg bw/day (maternal) NOAEL = 1,000 mg/kg bw/day (developmental)

Toxicokinetics, metabolism and distribution.
No toxicokinetic data were provided on the notified chemical. Based on the molecular weight and physic-chemical properties of the notified chemical, passive diffusion across the gastrointestinal (GI) tract and dermal absorption could occur (although the extent of absorption may be limited). The notified chemical may also be absorbed across the respiratory tract.

Acute toxicity.
The notified chemical was found to have low acute toxicity by the oral route in a study conducted in rats.

No acute dermal or inhalation toxicity data were provided for the notified chemical.

Irritation.
In an acute dermal irritation study in rabbits, a single 4-hour, semi-occluded application of the notified chemical resulted in erythema at all treated sites, with effects evident at the 1 hour observation after patch removal. At the 24 hour observation, erythema was noted in one animal only, with no responses recorded 48 hours after patch removal. No oedema was noted. The effects noted in this study were insufficient to warrant classification of the chemical as a skin irritant.

In a rabbit eye irritation study, conjunctival irritation was noted in all treated eyes from 1 hour after treatment, persisting at the 24 hour observation in one animal. Slight reddening of the sclera was also present in one animal at the 1 hour observation. The effects noted in this study were insufficient to warrant classification of the chemical as an eye irritant

Sensitisation.
A guinea pig maximisation test (using the Magnusson-Kligman method) was conducted to determine the skin sensitisation potential of the notified chemical in guinea pigs. Under the conditions of the study, the notified chemical (at 100% induction concentration; 1% challenge concentration) was found to be a non-sensitiser, with no responses noted in any animals at both the 24 and 48 hour observations after challenge patch removal.

Repeated dose toxicity.
In a 28-day repeated dose study in rats treated by oral gavage, the No Observed Adverse Effect Level (NOAEL) was established by the study authors as 1,000 mg/kg bw/day, based on the absence of adverse effects at the highest dose tested. Statistically significant effects were reported (various parameters), however, in general the effects were not considered by the study authors to be toxicologically significant and/or no dose-response relationship was evident.

Mutagenicity/Genotoxicity.
The notified chemical was not mutagenic in a bacterial reverse mutation study and non genotoxic to mouse lymphoma cells in an in vitro mammalian cell micronucleus test.

Developmental toxicity
A study to evaluate the developmental toxicity of the notified chemical was conducted in Wistar rats at 100, 300 and 1,000 mg/kg bw/day. Maternal rats dosed in the highest group showed reduced (statistically significant)

corrected body weight gain compared to the control animals. This was taken by the study authors to be indicative of slight maternal toxicity. In the foetuses, all abnormalities were deemed not toxicologically significant (and/or not adverse). Example effects noted in the foetuses included incidences of bilateral renal pelvis dilation (noted in the litters of all dose groups, however the study authors did not correlate a dose dependency) and an increased incidence of incomplete ossification of the coccygeal bone in the foetuses (noted in the foetuses of all dose groups; considered by the study authors to be a result of normal biological evaluation). Under the conditions of the study, the No Observed Adverse Effect Level (NOAEL) was established by the study authors as 300 mg/kg bw/day for maternal toxicity and 1,000 mg/kg bw/day for developmental toxicity.

Health hazard classification
Based on the available information, the notified chemical is not 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

Reformulation processes
Workers may experience dermal, ocular and perhaps inhalation exposure to the notified chemical (at ≤ 100% concentration) during reformulation processes. The notified chemical is considered to be slightly irritating to both the skin and eyes and based on the potential for toxicity effects following repeated exposure, caution should be exercised when handling the notified chemical during reformulation processes.

The use of enclosed, automated processes and PPE should minimise the potential for exposure. Provided that adequate control measures are in place to minimise worker exposure, 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 ≤ 15% concentration. Such professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. 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 on a regular basis (for details of the public health risk assessment, see Section 6.3.2.).

6.3.2. Public Health

Irritation
Skin and eye irritation effects are not expected from use of the notified chemical at the proposed concentrations in cosmetic products.

Systemic toxicity
The systemic toxicity potential of the notified chemical was estimated by calculation of the margin of exposure (MoE) using the worst case exposure scenario from use of multiple products of 5.243 mg/kg bw/day (see Section 6.1.2) and the NOAEL of 300 mg/kg bw/day, derived from the developmental toxicity study on the notified chemical. A MoE value ≥ 100 is generally considered acceptable to account for intra- and inter-species differences. Using the abovementioned NOAEL, a MoE of 57 was estimated, which is considered to be unacceptable. Eliminating use of the notified chemical in products to be applied by aerosol spray allows recalculation of the MoE to 92, which in this instance, is considered to be acceptable, due to the conservative nature of the exposure estimation.

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at ≤ 10% in body lotions and ≤ 15% in other cosmetic products (excluding products to be applied by aerosol spray) 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 will be 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.

During reformulation processes, limited release of the notified chemical is expected as blending will take place under industrial settings with engineering controls. Washings from cleaning of equipment are expected to be reused. A small amount of the notified chemical is expected to be generated as waste from residues in empty containers and spills during reformulation. Empty containers containing the notified chemical will either be recycled or disposed of through an approved waste management facility.

RELEASE OF CHEMICAL FROM USE

The majority of the notified chemical is expected to be released to the sewer across Australia as a result of its use in cosmetic products, which will be washed off the hair and skin of consumers and disposed of to the sewer. A small percentage of the notified chemical (≤ 3% of the total import volume), is expected to be disposed of to landfill as residues in empty end use containers.

RELEASE OF CHEMICAL FROM DISPOSAL

It is expected that some of the products containing the notified chemical will remain in end-use containers. The containers are expected to be disposed of through domestic garbage disposal and will enter landfill, or be subjected to recycling processes.

7.1.2. Environmental Fate

Following its use in Australia, the majority of the notified chemical is expected to enter the sewer before potential release to surface waters on a nationwide basis. The majority of the notified chemical will enter the sewer system as a result of the use of the notified chemical as a cosmetic ingredient in cosmetic products. Based on its predicted very high adsorption coefficient (log K_{oc} = 16.8 to 18.2), a significant partitioning to sludge is expected. The notified chemical has low potential to bioaccumulate based on its high molecular weight. In surface waters, the notified chemical is expected to disperse and degrade through biotic and abiotic processes to form water and oxides of carbon.

The notified chemical is expected to have low volatility from water (log H = 1.2 x 10^{-3} Pa/m^3/mol) and hence it is not likely to significantly volatilise to air during use or sewage treatment based on calculation for a representative component of the notified chemical. In the event of release to atmosphere, the notified chemical is not expected to persist in the air compartment based on calculations (AOPWIN v1.92; US EPA, 2011) for a representative component of the notified chemical.

A proportion of notified chemical may be applied to land when treated sewage effluent is used for irrigation or when sewage sludge is used for soil remediation, or disposed of to landfill. Notified chemical residues in landfill and soil are not expected to be mobile based on its high adsorption coefficient, and are expected to degrade to form water and oxides of carbon.

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 in cosmetic products, it is assumed that 100% of the total import volume of the notified chemical will be released to the sewer. The release is assumed to be nationwide over 365 days per year. It is conservatively assumed that 0% of the notified chemical will be removed during sewage treatment 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	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 1,000 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 1,500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.6 µg/L may potentially result in a soil concentration of approximately 4.0 µg/kg from each year of irrigation. 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 20.2 µg/kg and 40.4 µg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity data for the notified chemical were submitted. The ecotoxicity effects of the notified chemical were predicted using Ecological Structure Activity Relationship (ECOSAR v1.11, US EPA 2012). The conservative toxicity results are summarised in the table below.

Endpoint	Result	Assessment Conclusion
Fish	LC50 (96 h) < 1 mg/L	Not expected to exhibit toxic effect to fish at its water solubility limit
Daphnia	LC50 (48 h) < 1 mg/L	Not expected to exhibit toxic effect to aquatic invertebrates at its water solubility limit
Algae	EC50 (96 h) < 1 mg/L	Not expected to exhibit toxicity to algae at its water solubility limit

The measured water solubility of the notified chemical was 8.9×10^{-3} g/L. However, this value may only be representative of the soluble portions of the test substance due to the nature of the notified chemical being a complex mixture (discussed in Appendix A). Therefore, the measured data may not fully reflect the water solubility of the test substance as a whole. This assumption has been supported by the ECOSAR estimation of the toxicity values that the estimated endpoints indicate that the notified chemical may not be soluble enough to measure the predicted effect.

Classification should be based only on toxic responses observed in the soluble range. Furthermore, the actual toxicity of the notified chemical to aquatic life may be overestimated by ECOSARs estimation used here as surface waters tend to have higher total organic content (TOC) and dissolved organic content (DOC) than what is used in standard aquatic toxicity testing media. Classification should be based on actual toxicity endpoints and, therefore, the notified chemical cannot be formally classified under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) has not been calculated for the notified chemical as the notified chemical may not be soluble enough to measure the predicted effect. Since the notified chemical has high molecular weight and is highly hydrophobic in structure, it is expected to have very low water solubility. Based on its predicted very high log K_{oc} value, the majority of the notified chemical will be removed during STP processes by binding/sorption to sludge. Furthermore, the expected very small quantity of the notified chemical released to surface waters will be further removed by sorption to sediment in the receiving water. Therefore, the notified chemical is not likely to reach environmentally significant concentrations in the aquatic environment.

7.3. Environmental Risk Assessment

The notified chemical is expected to be biodegradable, although it is not readily biodegradable, and is not likely to bioaccumulate. Based on the predicted ecotoxicological data, the notified chemical is not expected to be

soluble enough in water to ever see the predicted toxicity effect levels reached in the environment. Based on the assessed use pattern of the notified chemical in cosmetic products, it is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Freezing Point - 20.5 °C to - 20.9 °C

Method	OECD TG 102 Melting Point/Melting Range.
Remarks	Determined using a dry ice/acetone bath.
Test Facility	RCC (2004a)

Boiling Point No boiling point up to 400 °C (decomposed before boiling).

Method	OECD TG 103 Boiling Point.
Remarks	Determined using a differential scanning calorimeter. No boiling point was observed up to 400 °C. Exothermic reactions (at ~ 230 and 350 °C) were noted, with a ~ 38% loss of mass.
Test Facility	RCC (2004b)

Water Solubility 8.9×10^{-3} g/L at 20 °C

Method	OECD TG 105 Water Solubility.
Remarks	Column Elution Method. The water solubility value may only be representative of the soluble portions of the test substance due to it being a complex mixture. Therefore, the result of this study may not reflect the water solubility of the test substance.
Test Facility	RCC (2004c)

Flammability Not “highly flammable”

Method	EEC Directive 92/69 A.10 Flammability (Solids).
Remarks	The test substance could not be ignited with a flame (contact time ~ 2 minutes). It melted immediately when in contact with an ignition source.
Test Facility	RCC (2004d)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
- Species/Strain: Rat/HanBrl: WIST
- Vehicle: Polyethylene glycol 300 (PEG 300)
- Remarks - Method: No significant protocol deviations. GLP Compliance.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3 per sex	2,000	0/6

- LD50: > 2,000 mg/kg bw
- Signs of Toxicity: No clinical signs were observed during the study period.
- Effects in Organs: No macroscopic findings were observed at necropsy in any of the test animals.
- Remarks - Results: No deaths occurred and all animals gained weight over the course of the study.

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

TEST FACILITY: RCC (2004e)

B.2. Irritation – skin

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 404 Acute Dermal Irritation/Corrosion.
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 2F/1M
- Vehicle: None
- Observation Period: 72 hours
- Type of Dressing: Semi-occlusive.
- Remarks - Method: No significant protocol deviations. GLP Compliance.

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	0.33	0	0	2	< 48 h	0
Oedema	0	0	0	0	NA	0

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

- Remarks - Results: Erythema was observed in all animals at 1 hour after patch removal, and persisted in the male animal, with erythema observed at the 24 hour observation.

CONCLUSION: The notified chemical is slightly irritating to the skin.

TEST FACILITY: RCC (2004f)

B.3. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 2F/1M
Observation Period 72 hours
Remarks - Method No significant protocol deviations.
GLP Compliance.

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0.33	0	0	1	< 48 h	0
Conjunctiva: chemosis	0	0	0	0	N/A	0
Conjunctiva: discharge	-	-	-	-	-	-
Corneal opacity	0	0	0	0	N/A	0
Iridial inflammation	0	0	0	0	N/A	0

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

Remarks - Results All animals displayed conjunctival redness at 1 hour after treatment and this continued in the male animal up to and including the 24 hour observation.
Slight reddening of the sclera was present in 1 of the females 1 hour after treatment.
The male animal showed decreased body weight from the day of treatment to the last day of observation. However the study authors considered the body weights of all animals to be within the normal range of variability.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY RCC (2004g)

B.4. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD OECD TG 406 Skin Sensitisation - Guinea-Pig Maximisation Test.
Species/Strain Guinea pig/Ibm:GOHI (Himalayan Spotted)
PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: 100%
topical: 1% in PEG 300
MAIN STUDY
Number of Animals Test Group: 10M Control Group: 5M
INDUCTION PHASE Induction Concentration:
intradermal: 100%
topical: 100%
Signs of Irritation Discrete/patchy to moderate/confluent erythema was observed in all animals at 24 hours after patch removal. Discrete/patchy erythema was noted in 7/10 animals at 48 hours after patch removal. No irritation was observed in control animals (treated with PEG 300).
CHALLENGE PHASE
1st challenge topical: 1% in PEG 300
Remarks - Method The vehicle was selected based on a preliminary solubility testing. The preliminary study used 7 male animals.
Challenge was performed on study day 27.
A concurrent positive control study was not conducted, but had been

previously conducted in the test laboratory using α-hexylcinnamaldehyde.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after challenge:*	
		24 h	*48 h*
Test Group	1%	0/10	0/10
	0%	0/10	0/10
Control Group	1%	0/5	0/5
	0%	0/5	0/5

Remarks - Results: No toxic symptoms or skin reactions (after challenge) were observed in any animal.

CONCLUSION: There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY: RCC (2004h)

B.5. Repeat dose toxicity

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
Species/Strain: Rat: Wistar Hannover
Route of Administration: Oral – gavage
Exposure Information: Total exposure days: 28 days
Dose regimen: 7 days per week
Vehicle: Corn oil
Remarks - Method: No significant protocol deviations.
GLP Compliance.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5 per sex	0	0/10
low dose	5 per sex	100	0/10
mid dose	5 per sex	300	0/10
high dose	5 per sex	1,000	0/10

Statistically significant slight variations in mean body weight gain were noted in both males and females as follows:

Treatment	Females	Males
1000	↑ mean body weight gain at week 1; ↓ mean body weight gain at week 2	
100	↓ mean body weight gain at week 2; (For week 1, the same numerical value for mean body weight gain was reported at this dose as at the high dose, however, this was not statistically significant).	↓ mean body weight gain at week 2

These effects were not considered by the study authors to be toxicologically significant due to the lack of a dose relationship and since there was no statistically significant effect on overall mean body weight gain.

Statistically significant changes in food consumption were noted at all dose levels in male animals and in mid and high dose females:

Treatment	Females	Males
1000	↓ mean food consumption at week 4	↓ mean food consumption at weeks 2

	only	and 4
300	↓ mean food consumption at week 4 only	↓ mean food consumption at weeks 1, 2, 3 and 4
100		↓ mean food consumption at weeks 2 and 4

These changes were not considered by the study authors to be test substance related (e.g. because they did not result in consistent effects on body weight gain).

Functional Observations

Statistically significant changes during open field evaluations were observed primarily in low dose male animals (and only slightly in high dose males, e.g. freezing time). No such changes were observed in females at any dose. In the functional observations, a statistically significant higher value for forelimb measures and landing foot spread/hindlimb foot splay were observed in males at the high dose which were not observed in female animals at any dose.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Statistically significant changes in measured haematological and clotting parameters were as follows:

Treatment	Females	Males
1000	↑ mean corpuscular haemoglobin; ↑ mean corpuscular haemoglobin concentration; ↓ absolute and relative eosinophil count; ↑relative monocyte count; ↓ prothrombin time	↓ haematocrit; ↑ mean corpuscular haemoglobin concentration; ↓ white blood cell count; ↓ absolute lymphocyte count; ↑ relative eosinophil count; ↓ prothrombin time
300	↓ relative eosinophil count	A higher value for relative eosinophil count was reported at this dose compared to the value for the high dose, however, at the mid dose, the value was not highlighted as statistically significant)

The above changes were deemed by the study authors as normal biological response without toxicological significance.

Statistically significant changes in clinical chemistry parameters were as follows:

Treatment	Females	Males
1000	↓ creatinine levels; ↓ albumin levels; ↑ potassium levels	↓ glucose levels; ↓ triglyceride levels
300	↑ alkaline phosphatase levels	↓ glucose levels
100	↑ total bilirubin levels	↑ sodium levels

These changes were not considered by the study authors to be treatment related and/or of biological concern, because they were either within the laboratory's historical range or they occurred only at mid and low doses.

Statistically significant changes in urinalysis parameters included increased density and increased level of ketones in low dose female animals.

Effects in Organs

Statistically significant changes in organ weights were as follows:

Treatment	Females	Males
1000	↑ absolute brain weight	↓ kidney weight (relative to brain weight)
300		↓ kidney weight (relative to brain weight)

The changes in kidney weight (relative to brain weight) seen in males showed a dose dependent response, though no statistical significance was attained in low dose male animals. In the absence of any microscopic lesions, these changes were not considered by the study authors to be toxicologically relevant.

There were no test substance and/or treatment related effects reported from macroscopic and microscopic examinations.

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) was established by the study authors as 1000 mg/kg bw/day in this study, based on the absence of adverse effects at the highest dose tested.

TEST FACILITY BIOAGRI (2014a)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD

	OECD TG 471 Bacterial Reverse Mutation Test. Plate incorporation (Test 1) and pre-incubation (Test 2) procedures
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98 and TA100 *E. coli*: WP2uvrA
Metabolic Activation System	S9 fraction from phenobarbitone/β-naphthoflavone induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 33, 100, 333, 1000, 2500 and 5,000 µg/plate b) Without metabolic activation: 33, 100, 333, 1000, 2500 and 5,000 µg/plate
Vehicle	Ethanol
Remarks - Method	No significant protocol deviations. GLP Compliance. A preliminary toxicity test (3-5,000 µg/plate; plate incorporation) was performed for all strains to determine the toxicity of the test material. The results are reported as Test 1. Positive control tests were conducted in parallel to the main test using sodium azide, 4-nitro-o-phenylene-diamine and methyl methane sulfonate in the absence of S9-mix, and 2-aminoanthracene with S9-mix.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	≥ 2,500	> 5,000	Negative
Test 2	> 5,000	> 5,000	Negative
Present			
Test 1	> 5,000	> 5,000	Negative
Test 2	> 5,000	> 5,000	Negative

Remarks - Results
No visible reduction in the growth of the bacterial background lawn was seen at any dose level, with and without metabolic activation. A minor toxic effect (reduction in the number of revertants) was observed on TA1535 at 2,500 and 5,000 µg/plate without S9 in Test 1 only.

No increases in the frequency of revertant colonies were recorded for any of the bacterial strains. No precipitate formation was observed.

The positive controls produced satisfactory responses, thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.

CONCLUSION The notified chemical was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY RCC (2004i)

B.7. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical

METHOD OECD TG 487 In vitro Mammalian Cell Micronucleus Test.
Species/Strain Mouse
Cell Type/Cell Line L5178Y TK$^{+/-}$ Mouse Lymphoma
Metabolic Activation System S9 fraction from Aroclor 1254.
Vehicle Ethanol
Remarks - Method No significant protocol deviations.
GLP Compliance.

A preliminary toxicity study was performed (3 hour exposure, with and without activation and 24 hour exposure without activation) at concentrations 5 – 2,500 µg/mL. Precipitate and/or emulsion were noted at the end of the treatment periods at ≥ 250 µg/mL.

Vehicle and positive controls (mitomycin C and colchicine without metabolic activation and cyclophosphamide with metabolic activation) were used in parallel with the test material.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Recovery Period*
Absent			
Test 1	9.38, 18.8*, 37.5*, 75*, 150 and 300	3 h	24 h
Test 2	9.38, 18.8, 37.5*, 75*, 150* and 300	24 h	20 h
Present			
Test 1	9.38, 18.8*, 37.5*, 75*, 150 and 300	3 h	24 h
Test 2	9.38, 18.8, 37.5*, 75*, 150* and 300	3 h	24 h

*Cultures selected for micronucleus analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 2500	> 300	≥ 75	Negative
Test 2	> 2500	> 300	≥ 150	Negative
Present				
Test 1	> 2500	> 300	≥ 75	Negative
Test 2		> 300	≥ 150	Negative

Remarks - Results In Test 1, in the presence of metabolic activation, a slight increase in the frequency of micronucleated cells was observed at 18.8 µg/mL. This increase was not statistically significant, not dose related and not reproducible in Test 2.

The positive and vehicle control values confirmed the validity of the test system.

CONCLUSION The notified chemical was not genotoxic to mouse lymphoma cells treated in vitro under the conditions of the test.

TEST FACILITY CIT (2013)

B.8. Developmental toxicity

TEST SUBSTANCE Notified chemical

METHOD OECD TG 414 Prenatal Developmental Toxicity Study
Species/Strain Rat/Wistar Hannover

Route of Administration	Oral – gavage
Exposure Information	Exposure days: days 6-19 of gestation
Vehicle	Corn oil
Remarks - Method	No significant protocol deviations. GLP Compliance.

RESULTS

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	25 F	0	0/25
low dose	25 F	100	0/25
mid dose	25 F	300	0/25
high dose	25 F	1,000	0/25

Effects on Dams

There were no unscheduled deaths or moribund/debilitated animals that needed to be sacrificed before necropsy. No clinical signs and macroscopic changes were observed in any dose groups. Gestational parameters were not affected in any dose groups. A slight maternal toxicity was noted at the high dose dams due to a statistically significant decrease in the corrected maternal body weight gain.

Effects on Foetuses

No treatment related variations or malformations were observed during external examination. No test item related foetal skeletal variations were observed.

The following statistically significant changes were noted:

Treatment	**Effect on foetuses**
1000	↑ bilateral renal pelvis dilation (litter basis); ↑ incidence of misshaped supraoccipital bone (foetal and litter basis); ↑ incidence of incomplete ossification of the coccygeal bone (foetal basis)
300	↓ mean placental weight (male foetuses); ↑ bilateral renal pelvis dilation (litter basis); ↑ incidence of incomplete ossification of the coccygeal bone (foetal basis)
100	↑ bilateral renal pelvis dilation (litter basis); ↑ incidence of incomplete ossification of the coccygeal bone (foetal basis)

The decreased mean placental weight was considered incidental since it was only seen in males in the mid dose group. The incidences of bilateral renal pelvis dilation were reported by the study authors to be slightly outside the historical control range, however, as there was no dose dependent relationship noted; and there were no other associated developmental changes, the effect was considered as non-adverse by the study authors. The higher incidence of misshaped supraoccipital bone was reported by the study authors to be within the historical control range. The higher incidence of incomplete ossification of the coccygeal bone observed in all treated groups was reported by the study authors to be common and spontaneous and was considered to be a result of normal biological variation.

CONCLUSION

The No Observed (Adverse) Effect Level (NO(A)EL) was established by the study authors as 300 mg/kg bw/day for maternal toxicity and 1,000 mg/kg bw/day for developmental toxicity.

TEST FACILITY BIOAGRI (2014b)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1 Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	Not reported
Analytical Monitoring	A respirometer was used for measurement of the consumption of oxygen (COD).
Remarks - Method	No significant protocol deviations. GLP Compliance..

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
2	10.5	2	56
14	38.5	7	82
28	57	28	97

Remarks - Results	All validity criteria for the test were satisfied. The reference compound, sodium benzoate, reached the 60% pass level by day 7 indicating the suitability of the inoculum. The toxicity control exceeded 25% biodegradation within 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The degree of degradation of the test substance after the cultivation period was 57% within 28 days. Therefore, the test substance cannot be classified as readily biodegradable according to the OECD (301 F) guideline.
CONCLUSION	The notified chemical is not readily biodegradable
TEST FACILITY	RCC (2002)

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