File No: LTD/1389

May 2009

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Laureth Carboxylic Acid

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (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 Ageing, 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, Water, Heritage and the Arts.

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at 334-336 Illawarra Road, Marrickville NSW 2204.

This Full 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:

Street Address:	334 - 336 Illawarra Road MARRICKVILLE NSW 2204, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
L'Oréal Australia Pty Ltd (ABN 40 004 191 673)
564 St Kilda Road
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: Chemical Name, Other Names, CAS Number, Molecular and Structural Formulae, Molecular Weight, Use Details and Impurities.

VARIATION OF DATA REQUIREMENTS (SECTION 24 O112F THE ACT)
Variation to the schedule of data requirements is claimed as follows: Boiling Point, Vapour Pressure, Hydrolysis as a function of pH, Partition Coefficient, Absorption/Desorption, Dissociation Constant, Flammability Limits, Auto-Ignition Temperature, Reactivity.

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Laureth Carboxylic Acid (INCI Name)
Akypo RLM 45 CA, (Kao GmbH)
Empicol CED 5/FL (Huntsman Holland BV)

OTHER NAME(S)
PEG-5 lauryl ether carboxylic acid, PEG-6 lauryl ether carboxylic acid, Laureth-5 carboxylic acid, Laureth-6 carboxylic acid.

MOLECULAR WEIGHT
< 700 Da.

ANALYTICAL DATA
Reference IR, GC spectra were provided.

3. COMPOSITION

DEGREE OF PURITY 87-99 %

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: Viscous colourless to light yellow liquid

Property	Value	Data Source/Justification
Melting Point	0-5°C	Measured
Boiling Point	Not determined	
Density	1,008 kg/m^3 at 20°C	Measured
Vapour Pressure	Not determined	
Water Solubility	< 10 g/L at 20°C	Measured
Hydrolysis as a Function of pH	Stable	MSDS
Partition Coefficient	Not measured	Unable to be tested due to surfactant properties

(n-octanol/water)		
Adsorption/Desorption	Not measured	Unable to be tested due to surfactant properties
Dissociation Constant	pKa ~ 5	Typical carboxylic acid.
pH	2.5 – 3.5 at 20°C	Measured
Flash Point	>100°C at 101.3 kPa	Measured
Flammability	Slightly flammable when in contact with naked flames, sparks or static discharge.	MSDS
Auto-ignition Temperature	Not determined	Not expected to auto-ignite under normal use conditions.
Explosive Properties	Not predicted to be explosive	The structural formula contains no explosophores.

DISCUSSION OF PROPERTIES

The notified chemical is a liquid which is described as insoluble in cold water but soluble in hot water. The true solubility is difficult to measure as the notified chemical is a surfactant that is easily dispersed in water through the formation of micelles. The surface activity precludes the measurement of partition coefficients, but indicates that some sorption to soil can be expected. It is expected to be of low flammability. For full details of tests on physical and chemical properties, please refer to Appendix A.

Reactivity

Potentially reactive or incompatible with alkali reagents.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL OVER NEXT 5 YEARS

Initially, the notified chemical will not be manufactured in Australia, but will be imported (≤ 15%) in cosmetic and household products. In future, the notified chemical may be imported as a raw material (80-90%) for reformulation into finished cosmetic and household products.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (80-90%) OVER NEXT 5 YEARS

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

PORT OF ENTRY

Port Melbourne, VIC

IDENTITY OF MANUFACTURER/RECIPIENTS

The notified chemical is made by Kao Chemicals GmbH, Kupferstrasse 1, D-46446 Emmerich Germany. Also made by Huntsman Holland BV, Rozenburg Works, Merseyweg 10, Rotterdam, The Netherlands.

TRANSPORTATION AND PACKAGING

Initially, the notified chemical will be imported as a component of finished cosmetic and household products in retail containers packed in cartons. They will be transported to the notifier's warehouse for distribution by road to retail warehouses and outlets for sale to the public.

In future, the notified chemical may be imported as an aqueous solution at 80-90% in 220 kg HDPE tanks housed in a galvanised steel container for use as a raw ingredient.

USE

The notified chemical will be used as a surfactant or cleansing agent (≤ 15%) in cosmetic and household products.

OPERATION DESCRIPTION

Finished cosmetic and household products containing the notified chemical will be used by consumers and in a professional setting by hairdressers and beauticians.

In future, the notified chemical may be imported as an aqueous solution (containing 80-90% notified

chemical). It will be transported to a reformulation site where it will be added to a mixing tank with other ingredients for reformulation into finished cosmetic and household products (containing ≤ 15% notified chemical). The formulation will be tested for quality assurance purposes before being packaged and distributed for retail sale.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

EXPOSURE DETAILS

Formulation

Accidental dermal and ocular exposure to drips, spills and splashes of the notified chemical (80-90%) may occur during quality assurance testing, charging of mixing vessels, mixing and filling of product packaging. The notifier states exposure is expected to be limited given the anticipated use of closed systems and personal protective equipment (PPE), such as safety goggles, impervious gloves and coveralls.

Inhalation exposure to aerosols is also possible during these processes. However, it is expected that exhaust ventilation will be in use to minimise exposure via this route.

Use of finished cosmetic products

Occupational exposure is possible for workers in hair and beauty salons using products containing the notified chemical (≤ 15%). Dermal exposure is expected to be extensive given that shampoo and cleansing products containing the notified chemical will be applied directly to the skin. Accidental ocular exposure and oral ingestion may also occur.

Although the level and route of exposure will vary depending on the method of application and work practices employed, extensive dermal exposure is expected in some occupational settings. This exposure is likely to be greater than that expected for the public (see below).

6.1.2. Public exposure

Public exposure to the notified chemical is expected to be widespread and frequent through daily use of cosmetic and household products containing the notified chemical at concentrations up to 15%. Exposure to the notified chemical will vary depending on individual use patterns. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray. Accidental ingestion from the use of these types of products is also possible from facial use.

Public exposure to the notified chemical in Australia has been estimated using the Scientific Committee on Consumer Products' (SCCP's) Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation and applying the following assumptions:

- Bodyweight of 60 kg for females (SCCP, 2006);
- The concentration of the notified chemical in all cosmetic and household products is 15%;
- 100% dermal absorption (SCCP, 2006);
- An individual uses all product types containing the notified chemical.

Product(s) used	*Use level for each product*	*Retention factor*	*Systemic Exposure (mg/kg bw/day)*
Facial cleanser	0.8 g x 0.5 applications/day	1.0	0.15
Shampoo	10.46 g per day	0.01	0.11
Conditioner	14.00 g x 0.28 applications/day	0.01	0.04
Shower gel	5.00 g x 2 applications/day	0.01	0.10
Laundry detergent[1]	230 g x 1 use/day	0.95	3.64
Dishwashing liquid[1]	28 g x 3 uses/day	1.0	0.29
Liquid soap[1]	1.6 g x 7 applications/day	0.50	0.93
Total product exposure =			5.26

Total exposure to the notified chemical at 15% in each of the products above = 5.26 mg/kg bw/day x 15%

Total	**0.79**

[1] Exposure estimates by the Soap & Detergent Association's (SDA) (2005).

This exposure estimate was produced using highly conservative assumptions and is expected to reflect a worst-case scenario. In reality, the level of exposure is expected to be lower than 0.79 mg/kg bw/day as it is assumed that consumers would not use all these products to the extent shown above.

6.2. Human health effects assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix B. Toxicological tests on a number of chemicals structurally similar to the notified chemical will also be discussed below.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	oral LD50 > 2000 mg/kg bw low toxicity
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	severely irritating
BCOP, eye irritation	moderately irritating
Guinea pig, skin sensitisation – adjuvant test.	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics

Limited data is available to describe the likely toxicokinetic properties of the notified chemical. It has low molecular weight (< 500 Da.), is water soluble (in hot water), ionisable and has surfactant properties. It may therefore be absorbed to some degree across biological membranes. Oral absorption studies on alcohol ethoxylates (which have similar ethoxylated carbon chains) found that these chemicals were absorbed in the GI tract and extensively and rapidly excreted in the urine. A small amount was excreted in faeces and expired air (as CO_2) (HERA, 2007). Dermal absorption studies on these chemicals found that significant amounts were absorbed through the skin of rats, but only small amounts (approximately 2%) through the skin of human volunteers (although this was a small study) (HERA, 2007). Although these chemicals do not contain the acid functionality of the notified chemical it may be expected that the notified chemical would act somewhat similarly and therefore may be extensively absorbed via the oral route and absorbed to a small extent via the dermal route.

Acute toxicity

The notified chemical was tested in an acute oral toxicity study in rats conducted according to OECD TG 401, the notified chemical was found to have an LD_{50} > 2000 mg/kg bw (Safepharm Laboratories Ltd, 1996). No mortality or signs of systemic toxicity were observed. Overall, the notified chemical was found to be of low acute toxicity following oral exposure. No data was available on the acute toxicity following dermal or inhalation exposure. Given the low dermal absorption expected the acute dermal toxicity is not anticipated to be greater than after oral exposure, and is therefore considered to be low.

Irritation and Sensitisation

The irritancy potential of the notified chemical was confirmed in a skin irritation test in rabbits conducted according to OECD TG 404. Very slight erythema was observed in all 3 animals at each observation point from 60 minutes until 10 days after application. Peeling of the epithelial layer was observed in all 3 animals from Days 9 to 12 (see Appendix B for further details).

The notified chemical (undiluted) was also found to be a severe irritant in an eye irritation test in rabbits conducted according to OECD TG 405, with corneal and iridial effects observed up to the end of the 20 day observation period (see Appendix B for further details). A bovine corneal opacity and permeability (BCOP) test was conducted on a product formulation containing the notified chemical at a concentration of < 15%. The test substance was applied as a 10% solution (therefore < 1.5% notified chemical). This diluted solution was found to be moderately irritating (see Appendix B for further details). The ICCVAM recommended protocol for the BCOP (ICCVAM, 2006) states that surfactant-based preparations (e.g. product formulations) are usually tested neat, or can be diluted with justification of the selected dilution. In this test the test substance was a surfactant-based preparation, but it was tested at 10% dilution rather than neat and no justification for this dilution is given in the study report. The BCOP is currently accepted as a valid screening assay to determine severe irritants, but has not yet been validated for distinguishing between non, mild, moderate and severe irritants.

The notified chemical does not contain any structural alerts for skin sensitisation (Barratt *et al*, 1994). Supporting this prediction, the notified chemical was not found to be sensitising in a skin sensitisation (maximisation) test in guinea pigs (see Appendix B for further details).

Repeated Dose Toxicity
No repeated dose toxicity data were submitted for the notified chemical. Numerous repeat dose toxicity studies via the oral and dermal routes have been conducted in rats on alcohol ethoxylates (which have similar ethoxylated carbon chains). In these studies, the effects observed were limited to changes in organ weights (with no histopathological changes) and hypertrophy of the liver (considered to be indicative of an adaptive response to metabolism rather than a toxic effect) (HERA, 2007). Therefore the notified chemical may be expected to have similar effects after repeat exposure, but a quantitative determination of the repeat dose toxicity cannot be made.

Mutagenicity
The notified chemical was found to be negative in a bacterial reverse mutation test conducted according to OECD TG 471 at concentrations up to 2,500 μg/plate in the absence and presence of metabolic activation (See Appendix B for further details).

Genotoxicity and Carcinogenicity
No data is available on the genotoxicity or carcinogenicity of the notified chemical. There was no evidence of genotoxic or carcinogenic potential in studies on alcohol ethoxylates (HERA, 2007).

Health hazard classification
Based on the effects observed in the rabbit eye irritation test, the notified chemical is classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004):

Xi; R41 Risk of serious eye damage

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
Irritation is the primary risk presented by the notified chemical to workers in occupational settings. The notified chemical was found to be severely irritating to the eye of rabbits when applied undiluted. At a concentration of < 1.5% the notified chemical was found to be moderately irritating to the eye in a BCOP test. The notified chemical was also found to be slightly irritating to the skin of rabbits when applied undiluted with evidence of inflammation persisting for > 10 days. Therefore, eye and to a lesser degree skin irritation, are potential risks to reformulation and/or transportation workers because of their handling of the notified chemical (80-90% concentration) prior to and during reformulation. Appropriate handling techniques and the use of PPE (safety goggles, gloves, coveralls) should be in place to minimise any of these risks to workers during handling and reformulation. The implementation of these measures would ensure the likelihood of exposure is very low and the risk to workers would therefore not be considered unacceptable.

Hairdressers and beauty therapists will encounter repeated dermal exposure to cosmetic products, such as shampoos, containing the notified chemical (≤ 15%). The risk of eye exposure is not considered likely given the hairdresser will normally be standing up during application of the shampoo to a client who is expected to be seated. The notified chemical was slightly irritating to the skin when tested undiluted in rabbits. While it is unknown whether irritation is likely after exposure at ≤ 15%, it is assumed that significant irritation would be unlikely given the rinse-off nature of the products containing the notified chemical.

6.3.2. Public health
Members of the public will experience widespread and frequent exposure to the notified chemical through daily use of cosmetic and household products (≤ 15%) which will involve direct contact with the skin and hair. There is potential for accidental eye exposure while using shampoo products containing the notified chemical (≤ 15%) and this could lead to eye irritation. This exposure could be either to the ≤ 15% formulation, or to a diluted shampoo solution. The notified chemical was found to be severely irritating (with corneal effects) undiluted and moderately irritating to a diluted product formulation (<1.5% notified chemical). As severe eye irritancy was observed with the undiluted chemical the potential for severe eye effects at

concentrations greater than 10% cannot be ruled out. At concentrations < 10% there is likely to be eye irritation, but this is less likely to be severe. Therefore although the notified chemical may cause some eye irritation when used in cosmetic and household products the risk of serious eye damage may be minimised by restricting the concentration to <10% and by clear and appropriate directions for use and safety precautions to avoid eye contact. First aid information should also be included on product packaging to minimise adverse effects if eye contact occurs.

Extensive dermal exposure to the notified chemical in cosmetic and household products at ≤ 15% is not considered to present an unreasonable risk of skin irritation given that the notified chemical was found to be only slightly irritating and is primarily intended for use in rinse-off products.

Members of the public will experience widespread and frequent exposure to the notified chemical through daily use of cosmetic and household products (≤ 15%). A maximum systemic exposure of 0.79 mg/kg bw/day was estimated. As no repeat dose toxicity studies have been conducted, a NOAEL could not be established for the notified chemical. Therefore a quantitative risk assessment cannot be conducted. However, given the expected low systemic toxicity after repeated use and the currently low introduction volume, the notified chemical is not expected to pose an unacceptable risk of systemic toxicity to the public when used in cosmetic and household products at ≤ 15%.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The notifier estimates that 3% of the imported quantity of the notified chemical could be washed to sewer when bulk containers are washed before recycling, and when formulation equipment is cleaned.

RELEASE OF CHEMICAL FROM USE
Essentially all of the imported quantity of the notified chemical will be washed to sewer as a result of its use in cosmetic and household products.

RELEASE OF CHEMICAL FROM DISPOSAL
Small amounts may be sent to landfill as residues in empty consumer containers, or washed to sewer when the containers are rinsed before recycling.

7.1.2 Environmental fate

No environmental fate data were submitted. The notified chemical is described as readily biodegradable on its MSDS, but the notifier does not have access to the supporting data. Ready biodegradability has been reported for ether carboxylic acids based on linear fatty alcohols (Behler *et al*, 1997). The notified chemical is expected to undergo some sorption to soil and sediment because of its surface activity. While the notified chemical may be expected to be mobile because of its high water solubility, any mobility will be limited by the ease of degradation. The water solubility and ease of degradation are expected to preclude any bioaccumulation in fish.

7.1.3 Predicted Environmental Concentration (PEC)

The PEC is calculated in the table below based on the worst case assumption that all will be discharged from sewage treatment works. In reality, losses are expected during sewage treatment due to biodegradation and sorption to sludge.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1000	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)	21.372	million
Removal within STP	0%	
Daily effluent production:	4,274	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.64	µg/L
PEC - Ocean:	0.064	µg/L

7.2. Environmental effects assessment

No ecotoxicity data were submitted. The MSDS reports a 96 hour LC50 of 7.5 mg/L in rainbow trout. This is consistent with the aquatic toxicity data evaluated for similar chemicals that have been notified to NICNAS.

7.2.1 Predicted No-Effect Concentration

A conservative PNEC can be estimated as tabulated below by application of an assessment factor of 1000 to the median acutely lethal concentration of 7.5 mg/L in rainbow trout.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
Rainbow trout 96 hour LC50	7.5	mg/L
Assessment Factor	1000	
PNEC:	7.5	µg/L

7.3. Environmental risk assessment

The risk quotients (Q = PEC/PNEC) are tabulated below.

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q – River	0.64	7.5	0.085
Q - Ocean	0.064	7.5	0.009

The notified chemical is not expected to pose a risk to the environment, based on its reported use pattern and the conservatively estimated risk quotients for fresh and marine waters.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification

Based on the available data the notified chemical is classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)]. The classification and labelling details are:

Xi; R41 Risk of serious eye damage

As a comparison only, the classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	***Hazard statement***
Serious eye damage	1	Danger: Causes serious eye damage
Acute aquatic toxicity	Acute 2	Toxic to aquatic life

Human health risk assessment

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

When used in cosmetic and household products, the notified chemical is not considered to pose an unacceptable risk to public health if used at < 10% with appropriate label statements regarding the potential for eye irritation.

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

Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- The Office of the ASCC, Department of Employment and Workplace Relations (DEWR), should consider the following health hazard classification for the notified chemical:
  - Xi; R41 Risk of serious damage to eyes

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - Concentration ≥ 10%: R41 Risk of serious damage to eyes
  - 5% ≤ concentration < 10%: R36 Irritating to eyes

  - The National Drugs and Poisons Standing Committee (NDPSC) should consider the notified chemical for listing on the SUSDP based on the results of eye irritation tests.

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced:
  - Avoid contact with eyes

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced:
  - Wear protective eyewear

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

- A copy of the MSDS should be easily accessible to employees.

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Public Health

- Consumer products containing the notified chemical should:
  - contain the notified chemical at less than 10% concentration;
  - be labelled with a warning against eye contact, and directions on first aid measures if the product enters the eye (e.g. avoid contact with eyes, in case of contact with eyes, rinse immediately with plenty of water and seek medical advice).

Disposal

- The notified chemical should be disposed of to landfill.

Storage

- The following precautions should be taken by L'Oréal Australia Pty Ltd regarding storage of the notified chemical:
  - Avoid contact with alkalis

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;
  - the concentration of the notified chemical in cosmetic products exceeds 10%;

or

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

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point 0-5°C

Method OECD TG 102 Melting Point/Melting Range.
EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks Pressure during the test is unknown
Test Facility Kao Chemicals GmbH (2007) (Report not provided)

Density 1008 kg/m^3 at 20°C

Method OECD TG 109 Density of Liquids and Solids.
EC Directive 92/69/EEC A.3 Relative Density.
Test Facility Kao Chemicals GmbH (2007) (Report not provided)

Water Solubility < 10 g/L at 20°C

Method Non guideline method.
Remarks A mixture of 1 g of the notified chemical and 100 mL of water formed a milky suspension at 25°C.

Hydrolysis as a Function of pH

Method Test not conducted.
Remarks The notified chemical contains no readily hydrolysable functionality and has been shown to be stable in commercial use over a wide pH range (3-9).

Partition Coefficient (n-octanol/water) Not measured

Remarks Measurement of the partition coefficient would be confounded as the notified chemical is surface active and would not form a clean partition.

Adsorption/Desorption Not measured

Remarks The measurement of soil adsorption would be confounded as the notified chemical is surface active. The surface activity is expected to entail some adsorption to soils, notwithstanding the high water solubility.

Dissociation Constant pKa ~ 5

Remarks The dissociation constant was not measured, but is expected to be typical for a carboxylic acid.

Particle Size

Method OECD TG 110 Particle Size Distribution/Fibre Length and Diameter Distributions.

Remarks Using a sieving and laser diffraction method the particle size of a 95% low water version of the notified chemical, the mass median diameter (MMD) was determined to be 72.2µm.
The particle size distribution was found to range from approximately 0.5-500µm.
Test Facility RCC Ltd (2005) (Report not provided)

Flash Point > 100°C at 101.3 kPa

Method EC Directive 92/69/EEC A.9 Flash Point.

Test Facility	Huntsman Holland BV (2006) (Report not provided)

Viscosit 500 cP at 20°C

Method	In house method for viscosity of liquids
Test Facility	Kao Chemicals GmbH (2007) (Report not provided)

pH 2.5-3.5 at 20°C

Method	Huntsman Analytical Method G9E1 Issue 9 24 August 1992.
Test Facility	Huntsman Holland BV (2006)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Irritation – skin

TEST SUBSTANCE: Notified chemical undiluted

METHOD: OECD TG 404 Acute Dermal Irritation/Corrosion.
EC Directive 92/69/EEC B.4 Acute Toxicity (Skin Irritation).

Species/Strain	Rabbit/Himalayan
Number of Animals	3 Males
Vehicle	Applied undiluted
Observation Period	13 days
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.

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	1	1	1	1	< 11 days	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 at each observation point between 60 minutes and 10 days after patch removal in all 3 animals. On the 7th and 8th day after patch removal, epidermal fissures were observed in all 3 animals. Peeling of the epithelial layer was observed from Day 9 to Day 12 in all 3 animals.

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

TEST FACILITY: Laboratory of Pharmacology and Toxicology (1995a)

B.2. Irritation – eye

TEST SUBSTANCE: Notified chemical undiluted

METHOD: OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).

Species/Strain	Rabbit/Himalayan
Number of Animals	3 Females
Observation Period	20 Days
Remarks - Method	No significant protocol deviations.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	2	2	2	2	20 days	1
Conjunctiva: chemosis	2	1	1	2	< 14 days	0
Conjunctiva: discharge	1	1	1	1	< 7 days	0
Corneal opacity	1	1	1	2	20 days	2
Iridial inflammation	1	1	1	2	20 days	2

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

Remarks - Results	Conjunctival redness (grade 1 and 2) was observed from 1 hour onwards in all 3 animals and persisted until 20 days after treatment in 2 animals. Conjunctival chemosis (grade 1 and 2) was observed in all 3 animals starting from 1 hour in 2 animals and persisting until 12 days after treatment in 1 animal. A white conjunctival hypersecretion was observed in all 3 animals from 1 hour after treatment up to 6 days after treatment. Corneal opacity (grade 1 and 2) was observed from 24 hours until 20 days after treatment in all 3 animals. Tests with fluorescein confirmed the corneal effects which affected the entire area. Pericorneal vascular injection was observed in 2 animals on Day 12 and pericorneal vascular injection, commencing detachment of the cornea, was observed from Day 13 to Day 19 in 1 animal. In addition, detachment of the cornea was observed in 1 animal on Day 20. Iridial inflammation was observed in all 3 animals from 24 hours to 20 days after treatment and was characterised by markedly deepened rugae, congestion, swelling, moderate circumcorneal hyperaemia or injection, haemorrhages and/or gross destruction. The iris still reacted to light (at grade 1).
CONCLUSION	The notified chemical is severely irritating to the eye.
TEST FACILITY	Laboratory Pharmacology and Toxicology (1995b)

B.3. Irritation – eye

TEST SUBSTANCE	489777 A (shampoo containing the notified chemical at < 15%)
METHOD	Adaptation of Bovine Corneal Opacity and Permeability (BCOP) test as described by Gautheron, P., et al., (1992) *Fundamentals of Applied Toxicology*, 18, pp. 442-449.
Species/Strain	Bovine
Number of Animals	3 corneas
Observation Period	2 hours
Remarks - Method	Bovine eyes were excised by making an incision into the scleral ring. Six corneas were kept for a maximum of 24 hours in a preservative medium stored at 4°C. The corneas were placed epithelial side upwards on cornea holders and clamped in place with 3 screws. The compartments housing the epithelial and endothelial sides were filled with nutritive medium. The corneal holder was placed in a bain-marie immersed at three-quarters of their height at a temperature of 32°C for 1 hour. After this period, the light flow transmission through the cornea was determined using an opacitometer. After pre-incubation, the contents of the compartments were removed with suction. The endothelial compartment was filled with nutritive medium and the epithelial compartment of 3 test corneas was filled with 750 µL of a 10% solution of the test substance (< 1.5% of the notified chemical) and the epithelial compartment of the 3 negative control corneas was filled with 750 µL of nutritive medium. After incubation at 32°C for 30 minutes in a bain-marie the contents of the compartments were removed with suction and rinsed 3 times with 2 mL of nutritive medium. The epithelial compartment was filled with 1 mL of a fluorescein solution and the endothelial compartment was filled with nutritive medium. The corneal holders were incubated in a bain-marie for 1 hour 30 minutes at a temperature of 32°C. After incubation, the fluorescein in the epithelial compartment was removed with suction and the medium in the endothelial compartment was removed with a syringe needle.

Optical Density: The contents of the two compartments were placed in a cuvette and the optical density was measured with a spectrophotometer at 490 nm. The value for each cornea was obtained for the 3 corneas treated with the test item and the 3 negative control corneas.
The corneas were examined for any visible modifications following treatment.
Optical Transmission: Measurements were performed to determine the difference in the light flow transmission through the cornea before and after treatment using an opacitometer.
A corneal score was obtained based on the following equation:
Corneal score = mean adjusted Optical Transmission (OT) + 15 x mean adjusted Optical Density (OD).

The method used was similar to that recommended by ICCVAM in their evaluation and validation of the BCOP assay (ICCVAM, 2006), except for the following:

- The exposure time recommended by ICCVAM is 10 minutes (30 minutes was used in this test;
- The ICCVAM method states that surfactant-based preparations (e.g. product formulations) are usually tested neat, or can be diluted in 0.9% sodium chloride, with justification of the selected dilution. In this test the test substance was a surfactant-based preparation, but it was tested at 10% dilution rather than neat and no justification for this dilution is given in the study report.

RESULTS

Lesion	*Mean Adjusted Score*			*Mean Value*
	1	2	3	
Optical Transmission	2.3	0.3	1.3	1.3
Optical Density	1.019	1.167	0.894	1.027
Corneal Score	17.6	17.6	14.7	16.7

Remarks - Results

A mean corneal score of 16.7 ± 1.7 was obtained after treatment with the diluted test substance for 30 minutes. This result falls within the range 10-25, indicating that the test substance (diluted product formulation) was moderately irritating (Class 2).

No visible affects to the cornea were reported by the study authors.

A positive control substance was tested within 1 month of this study and was found to give the appropriate response.

CONCLUSION

The diluted test substance (<1.5% notified chemical) was found to be moderately irritating to the eye.

TEST FACILITY

L'Oréal (2008)

B.4. Skin sensitisation

TEST SUBSTANCE

Notified chemical undiluted

METHOD

OECD TG 406 Skin Sensitisation – Magnusson and Kligman

Species/Strain

Guinea pig/Dunkin-Hartley

PRELIMINARY STUDY

Maximum Non-irritating Concentration:
intradermal: 0.1% in 0.9% NaCl solution
topical: 0.01% in 0.9% NaCl solution

MAIN STUDY

Number of Animals	Test Group: 10 Control Group: 10
INDUCTION PHASE	Induction Concentration: intradermal: 0.5% in 0.9% NaCl solution topical: Undiluted
Signs of Irritation	Very slight irritation was observed up to 72 hours after intracutaneous injection into the shoulder with 0.5% notified chemical in 0.9% NaCl solution.
CHALLENGE PHASE	
1st challenge	topical: 0.01% in 0.8% hydroxypropyl-methylcellulose gel
Remarks – Method	No significant protocol deviations.

RESULTS

Remarks - Results	A positive control test (Dunkin-Hartley Guinea pigs) was conducted using 10 animals treated with Potassium dichromate solution in the following concentrations in distilled water for induction: 1.0% (intradermal injection) and 1.0% (topical application). Reactions ranging from no erythema to moderate-severe erythema were observed in animals 72 hours after topical challenge with 0.1% Potassium dichromate solution indicative of a contact sensitisation reaction. However, Potassium dichromate is one of the strongest known sensitisers and it is unclear whether this test method is suitable for detecting weaker sensitisers.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	Laboratory of Pharmacology and Toxicology (1995c)

B.5. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100
Metabolic Activation System	S9 fraction from Aroclor 1254 induced rat liver.
Concentration Range in Main Test	a) With metabolic activation: 4 - 2,500 µg/plate b) Without metabolic activation: 4 - 2,500 µg/plate
Vehicle	Water
Remarks - Method	The test was only conducted in *S. typhimurium* strains. Therefore the mutagenicity to other bacterial species could not be ascertained. No other significant protocol deviations

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	2,500	None	Negative
Test 2	-	2,500	None	Negative
Present				
Test 1	5,000	2,500	None	Negative
Test 2	-	2,500	None	Negative

Remarks - Results	Visibly reduced or complete reduction of background lawn was observed in all strains treated with 2,500 µg/plate in the absence and presence of metabolic activation. No substantial increase in revertant colony numbers of any of the tester strains were observed following treatment with the notified chemical at any dose level, with and without metabolic activation, in either mutation test. The concurrent positive control compounds (Sodium Azide, 9-Aminoacridine, 2-Nitrofluorene (-S9), 2-Aminoanthracene (+S9)) demonstrated the sensitivity of the assay and the metabolising activity of the liver preparations.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Toxicol Laboratories Limited (1984)

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