File No: SN/21

March 2011

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Glycine, N-coco acyl derivs., sodium salts (Sodium Cocoyl Glycinate)

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 Sustainability, Environment Water, Population and Communities.

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 Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

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:

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Director
NICNAS

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FULL PUBLIC REPORT

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Unilever Australia Limited (ABN: 66 004 050 828)
20 Cambridge Street
Epping, NSW 2121

Amtrade International Pty Ltd (ABN: 49 006 409 936)
574 St Kilda Rd
Melbourne, VIC 3004

Assessment of the notified chemical was carried out under the *Industrial Chemicals (Notification and Assessment) Act 1989* [the IC(NA) Act], as LTD/1306, with the Summary Report of the assessment published in the *Chemical Gazette* of 7th August, 2007. An extension of the assessment certificate (EX/130) was subsequently conducted with the Summary Report of the assessment published in the *Chemical Gazette* of 7th September, 2010.

The Director of NICNAS was informed of an increase in the introduction volume of the notified chemical in excess of the permitted volume under the limited category (1 tonne/annum). Under the IC(NA) Act, the Director declared that a secondary notification was required for the chemical known as Glycine, N-coco acyl derivs., sodium salts (Sodium Cocoyl Glycinate).

In accordance with Section 65 of the IC(NA) Act, a notice requiring the secondary notification of Glycine, N-coco acyl derivs., sodium salts (Sodium Cocoyl Glycinate) was published in the *Chemical Gazette*. The notice of 7th December, 2010 stipulated that the following data were required to undertake further assessment of Glycine, N-coco acyl derivs., sodium salts (Sodium Cocoyl Glycinate):

Any changes in the following data items from that submitted in the original notification:

1. Identity, Properties and Uses

    a) proposed uses of the chemical;
    b) concentration of the chemical in end-use products;
    c) import quantity (and changes to occupational exposure for workers); and
    d) physico-chemical properties.

2. Toxicity

Human health:
    a) the chemical's toxic effects following single dermal and inhalation exposure;
    b) the chemical's toxic effects following repeated exposure;

Ecotoxicity:
    c) the toxicity of the chemical to fish;
    d) the toxicity of the chemical to aquatic invertebrates;
    e) the effects of the chemical on algae;
    f) additional data related to the chemical's biodegradability and potential to bioaccumulate.

Any additional available data on the toxicological and/or environmental effects of the chemical should also be provided. The requested data may be provided through the submission of studies (tests conducted on the notified chemical or suitable analogue) or other sources of information.

This report, SN/21, represents the revised assessment for Glycine, N-coco acyl derivs., sodium salts (Sodium Cocoyl Glycinate). In addition to an increase in introduction volume, the assessment also covers a proposed increase in the concentration of the notified chemical in end-use products. Where additional data has been provided, it has been incorporated into the report and the implications of the data for the health and

environmental risks of the notified polymer considered.

NOTIFICATION CATEGORY
Secondary Notification

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

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: Melting Point, Vapour Pressure, Water Solubility, Hydrolysis as a Function of pH, Dissociation Constant, Flammability Limits, Auto ignition Temperature, Explosive Properties, Reactivity

PREVIOUS NOTIFICATIONS IN AUSTRALIA BY APPLICANT(S)
LTD/1306
EX/130

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

CHEMICAL NAME
Glycine, N-coco acyl derivs., sodium salts

OTHER NAME(S)
Sodium Cocoyl Glycinate

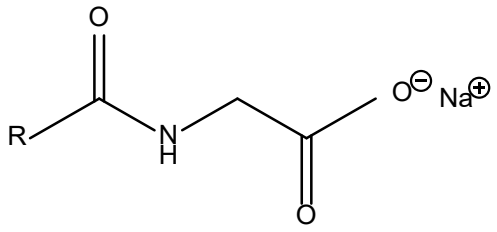
MARKETING NAME(S)
Amilite GCS-11
Amilite GCS-12
Extension Application:
Amilite GCS-11 (product containing the notified chemical at ≥87% concentration)

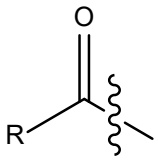
CAS NUMBER
90387-74-9

MOLECULAR FORMULA
The notified chemical is a mixture of glycine N-acyl derivatives of fatty acids from coconut oil. Main component (47%) represents the derivative of the lauric acid.

$C_{14}H_{26}O_3N\ Na$ (as lauroyl derivative)

STRUCTURAL FORMULA



where 

is Cocoyl from coconut oil

MOLECULAR WEIGHT
279 Da as lauroyl derivative

ANALYTICAL DATA
Reference IR, spectra was provided
Summary HPLC study was provided
Component derivatives in the Amilite GCS-11 mixture:

47% lauroyl derivatives C12
18% myristoyl derivatives C14
9% palmitoyl derivatives C16
6% capryloyl derivatives C10
6% oleoyl derivatives C18:1
2% linoleoyl derivatives C18:2
3% stearoyl derivatives C15

3. COMPOSITION

DEGREE OF PURITY
>87% for Amilite GCS-11 (powder)
Amilite GCS-12 is a 31.5% water solution of Amilite GCS-11 containing 27.4% of notified chemical

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (>1% by weight)

Chemical Name	Cocoyl Fatty Acid		
CAS No.	61788-47-4	*Weight %*	9% maximum
Chemical Name	Sodium Sulfate		
CAS No.	7757-82-6	*Weight %*	2.5% maximum
Chemical Name	Sodium Chloride		
CAS No.	7647-14-5	*Weight %*	1.5% maximum
Chemical Name	Water		
CAS No.	7732-18-5	*Weight %*	1% maximum

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20ºC and 101.3 kPa White to light yellow powder

Property	Value	Data Source/Justification
Melting Point	32-34 ºC	MSDS
Boiling Point	Not provided	Decomposition occurs at temperatures above 150ºC
Density	Not provided	
Vapour Pressure	$<10^{-5}$ kPa	Estimated
Water Solubility	<0.5% w/w at 25°C	Measured
Hydrolysis as a Function of pH	Not provided	The notified chemical contains hydrolysable functionality. However, based on the biodegradability test report (provided in Japanese only), it would appear that hydrolysis was not observed in the 28 d test period.
Partition Coefficient (n-octanol/water)	log Pow = 0.158 – 3.89	Calculated using KOWWIN (v1.67) (US EPA, 2009) for ionised and unionised forms of the notified chemical. The notified chemical is a surfactant and expected to concentrate at phase boundaries.
Adsorption/Desorption	Not provided	Based on the structure, appreciable adsorption to organic carbon, soil and sediments could be expected.

Dissociation Constant	pKa = 4.64-5.86	Estimated based on main components of the notified chemical, namely Sodium Lauroyl Glycinate and Sodium Myristoyl Glycinate
Particle Size	Inhalable fraction (<100 μm): <23 % Respirable fraction (<10 μm): <9.6 % D50 average 126 μm	Measured
Flash Point	Not provided for solid	
Flammability	Not provided	
Autoignition Temperature	Not provided	
Explosive Properties	Not determined	The notified chemical does not contain chemical groups expected to be explosive

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

Reactivity
The notified chemical is expected to be stable under normal environmental conditions. No test of oxidising properties was performed. The notified chemical does not have any structural indications of oxidising properties or other unusual activity.

The CIR compendium and report (CIR 2001, 2004) on the analogue chemicals acyl sarcosines raised concern about the possible formation of potentially carcinogenic nitrosated derivatives. For the analogue, the reactive material is likely to be the precursor sarcosine. The situation for the notified chemical varies in that the precursor amine glycine is a primary amine, whereas the precursor amine sarcosine in the analogue material is a secondary amine. Secondary amines are of more concern for nitrosamine formation than primary or tertiary amines. Whereas the nitrogen in the notified chemical itself (coco acyl glycinate) is secondary, its functional group is an amide rather than an amine and has different chemical properties. Free amine is not present in the notified chemical, based on the information supplied for the assessment. Therefore the possibility of nitrosamine formation in the notified chemical is considered to be low.

Dangerous Goods classification
Based on the submitted physico-chemical data in the above table the notified chemical is not classified according to the Australian Dangerous Goods Code (NTC, 2007). However the data above do not address all Dangerous Goods endpoints. Therefore consideration of all endpoints should be undertaken before a final decision on the Dangerous Goods classification is made by the introducer of the chemical.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. It will be imported as a component (≤15%) of finished cosmetic products and as a raw material Amilite GCS-11 (87% notified chemical) or Amilite GCS-12 (27% notified chemical) for local formulation into end-use products

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

Year	*1*	*2*	*3*	*4*	*5*
Tonne	45	45	45	45	45

PORT OF ENTRY
Sydney or Melbourne by wharf or air

IDENTITY OF MANUFACTURER/RECIPIENTS
Unilever Australia Limited and Amtrade International Pty Ltd

TRANSPORTATION AND PACKAGING
The finished products containing the notified chemical (at ≤15%) will be imported in ≤200 mL containers suitable for retail sale. These bottles will be packaged in cardboard cartons packed 12 per cardboard shipper.

The shippers with finished products containing the notified chemical will be transported in a container from the wharf to the Unilever Australia Limited's central warehouse at Ingleburn, NSW. The cartons will be transported to retail stores' distribution centres by road.

The raw material (≤87% notified chemical) will be imported into Australia in 15 kg carboy pack with inner lining and will be transported within Australia by road to the notifiers warehouse.

USE
The notified chemical will be used as a component of cosmetic and personal care products. It will be used in a variety of rinse-off (at ≤15% concentration) and leave-on (at ≤5% concentration) products.

OPERATION DESCRIPTION
The notified chemical will be introduced into Australia as a component of finished cosmetic products and as a raw material. The finished products will be warehoused and transported to retail outlets, where they will be sold to consumers.

Reformulation of the raw material (≤87% notified chemical) will occur at various sites within Australia. The reformulation will include transfer of the notified chemical from the 15 kg containers and mixing with other cosmetic ingredients followed by packaging into the small 200 mL containers that will be distributed to consumers. Mixing and dispensing will be carried out in a closed system or under conditions designed not to create aerosols or to generate airborne dust.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure assessment

6.1.1. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration h/day*	*Exposure Frequency Days/year*
Transport and Storage	10	4	12
Reformulation workers	1	8	36
Quality control Chemist	1	3	36
Packers (Dispensing and Capping)	2	8	36
Store Persons	2	4	36

Exposure Details

Reformulation

Dermal, ocular and inhalation (aerosol) exposure of workers to the notified chemical as imported may occur during opening of the import containers, weighing and transferring the notified chemical into a mixing vessel, and connecting and disconnecting transfer and filling lines. There is also potential for inhalation exposure to dusts of the notified chemical when handling and weighing the imported powdered raw material of the notified chemical. Dermal and ocular exposure to the notified chemical (up to 15% concentration) may also occur during quality control operations, and dispensing of the reformulated product into end use containers. Exposure is expected to be lowered by the enclosed nature of the mixing vessel, the automated systems used for mixing and dispensing, the use of exhaust hoods, and the wearing of personal protective equipment (PPE), that may include overalls, face-mask or safety glasses, safety shoes, gloves and respiratory protection (if ventilation is inadequate).

End-Use

Dermal, ocular, and inhalation exposure to the notified chemical (at concentrations up to 15%) may occur in professions (e.g. hair dressers, workers in beauty salons) where the services provided involve the application of personal care products. Such professionals may use some personal protective equipment to minimise 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

Public exposure is expected to be widespread and frequent through the daily use of cosmetic and personal care

products containing the notified chemical at concentrations ≤15%.

The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray. Oral exposure is only possible in case of accidental ingestion of products containing the notified chemical.

6.2. Human health effects assessment

The results from toxicological investigations conducted on the notified chemical and on acceptable analogues of the notified chemical are summarised in the table below. Details of these studies can be found in Appendix B.

The analogue chemicals (1 and 2 below) are acceptable based on the structural similarity with the notified chemical.

Analogue 1 (the potassium salt of the notified chemical): Glycine, N-coco acyl derivs., potassium salts (CAS number: 301341-58-2)
Analogue 2 (contains approximately 80% analogue 1): Fatty acids, coco, reaction products with glycine, potassium salts (CAS number: 1170699-53-2)

In addition, some published information from the Cosmetic Ingredient Review (CIR) on modified fatty acids known as acyl sarcosines and sarcosinates that are structurally related to the notified chemical is included in the health effects assessment, e.g. Sodium Lauroyl Sarcosinate.

Endpoint	*Result and Assessment Conclusion*
Mice, acute oral toxicity	LD50 >2000 mg/kg bw; low toxicity
Rabbit, skin irritation	Slightly irritating at 5% concentration
Rabbit, skin irritation[1]	Slightly irritating at 5% concentration
Rabbit, skin irritation[2]	Irritating at tested concentration (assumed to be up to 30%)
Rabbit, eye irritation	Irritating at 5% concentration
Rabbit, eye irritation[1]	Irritating at 5% concentration
Rabbit, eye irritation[2]	Irritating at tested concentration (assumed to be up to 30%)
Guinea pig, skin sensitisation – adjuvant test	No evidence of sensitisation at 5% concentration
Genotoxicity – bacterial reverse mutation	Non mutagenic
Genotoxicity – in vitro Chromosome Aberration Test in hamster lung fibroblasts (CHL/IU)	Genotoxic in the presence of metabolic activation
Genotoxicity – in vivo Mammalian Erythrocyte Micronucleus Test	Non genotoxic

[1]Study conducted on analogue chemical 1
[2]Study conducted on analogue chemical 2

Toxicokinetics, metabolism and distribution
Information on the absorption, metabolism and excretion of the notified chemical was not provided. The notified chemical represents a Sodium salt of an N-acyl glycine acyl derivative of the mixture of fatty acids from coconut oil with surfactant properties and low water solubility (<5% w/w). N-acyl derivatives of sarcosine (acyl sarcosines) and their salts (sarcosinates) are structurally similar to the notified chemical and are also used as surfactant-cleansing agents in cosmetic products. A skin permeability test on rats revealed that acyl sarcosines and sarcosinates enhanced the skin absorption of other ingredients when applied together in the same formulation (CIR, 2001). Due to this finding, cosmetic products containing the notified chemical should be carefully formulated to avoid combining with other ingredients (including colourants and dyes) if transdermal absorption is a health concern. The structurally related chemical, Sodium Lauroyl Sarcosinate, is reported as not being hydrolysable by either gastric or intestinal enzymes *in vitro*. In a metabolism study in rats, 82%-89% of a 50 mg/kg oral dose of Sodium Lauroyl Sarcosinate was excreted in the urine and faeces within 24 hours, and 1%-2% was excreted over the next 24 hours (CIR, 2001), suggesting that it is not readily absorbed through the gastrointestinal wall. In an oral dosing study in rats, radiolabelled Sodium Lauroyl Sarcosinate was administered and tissue samples (including urine and faeces) were analysed. At 24 hours after administration, 42% was present in the urine and less than 2% were found in organs such as the liver, kidneys, teeth and oral mucosa. Around 1% of the compound remained adhered to the teeth, oral mucosa and tongue and the radioactivity could

not be washed out by physiological saline, indicating that Sodium Lauroyl Sarcosinate was absorbed into the blood. However, the uptake is not permanent according to a different study, which found that frequent application did not cause an accumulation of radiolabelled sarcosinate in bone or muscle (CIR, 2001). The notified chemical is likely to have similar absorption, metabolism and elimination kinetics to sarcosinates and are not likely to lead to bioaccumulation.

Acute toxicity
The notified chemical was of low acute oral toxicity with LD50 >2000 mg/kg bw as determined in a limit test in mice.

No data were provided on the acute dermal toxicity of the notified chemical. A study involving dermal application of Sodium Lauroyl Sarcosinate on the skin of rabbits for 14 days was reported to result in no signs of dermal toxicity. This suggests that the notified chemical is of low acute dermal toxicity.

The acute inhalation toxicity or potential for respiratory irritation of the notified chemical is unknown. In addition, there is no data available on the inhalation toxicity of acyl sarcosines or sarcosinates.

Irritation and sensitisation
The notified chemical caused slight irritation to the skin of rabbits when tested at 5%, Considering the mean erythema score was 1.83 at this tested concentration, the notified chemical at 100% is expected to have severe irritation effects and should be classified as at least a skin irritant. This is further supported by two skin irritation tests conducted on the analogue chemicals. The first test, which was conducted using analogue chemical 1, showed similar results at 5% to the notified chemical, with a result of slightly irritating to rabbit skin. The second test, which was conducted using analogue chemical 2, showed the chemical to be irritating to skin when tested at up to 30% concentration.

The notified chemical does not contain a structural alert for sensitization and there was no evidence of skin sensitization in a guinea pig maximization study when induced and challenged at a concentration of ~5%.

The notified chemical caused slight irritation to the eyes of rabbits when tested at 5%. However, mild redness of the conjunctivae was persistent and was not reversible even after 7 days in 3/6 animals. Considering the irritant effects observed at 5% concentration, the notified chemical at higher concentrations should be classified as a severe eye irritant. This is further supported by two eye irritations tests conducted on the analogue chemicals. The first test, which was conducted using analogue 1, showed similar results at 5% to the notified chemical with a result of slightly irritating to rabbit eyes. The second test, which was conducted using analogue chemical 2, showed it to be irritating to rabbit eyes when tested at up to 30% concentration. In the study with analogue 2, significant eye irritation was observed, particularly conjunctival redness. Based on the severity of the effects, the study authors decided to test only one animal.

Subchronic and chronic toxicity
No information on repeat dose toxicity was available for the notified chemical. Weanling rats given a diet containing 2% Sodium Lauroyl Sarcosinate for 6 months had no effect on weight gain, feeding, general health or behaviour (CIR 2001). There were no abnormalities of the internal organs. Rats fed 0.5% Sodium Lauroyl Sarcosinate for 100 days also showed no signs of toxicity. In a chronic toxicity study, 200 albino Wistar rats were fed Sodium Lauroyl Sarcosinate ranging from 0.05% to 2.0% for a period of 2 years. There were no significant differences in lesions, fertility, mortality, haematology or body weight gain between the control and treated groups. The only significant change after 24 months was minor hyperplasia of the stratified squamous epithelium and excess keratin formation in the stomach mucosa of rats treated at the highest doses (1% and 2%) (CIR 2001). It is expected that the notified chemical may have similar repeat dose toxicity to that described above for Sodium Lauroyl Sarcosinate.

Reproductive Effects
Information on Sodium Lauroyl Sarcosinate indicated that rats fed up to 1000 mg/kg/day did not experience adverse effects on fertility in a 2-year oral toxicity study (CIR 2001).

Mutagenicity
The notified chemical was not mutagenic to bacteria in the Ames test in the presence or absence of metabolic activation. It also was not clastogenic in a Chromosomal Aberration test using Mammalian lung fibroblasts in the absence of metabolic activation but it increased the percentage of cells with aberrations in the presence of metabolic activation at the highest concentration tested. Based on this result the notified chemical is considered

to be clastogenic to mammalian cells in vitro the presence of metabolic activation. However, the significance of the positive result is unclear as the increase of aberrations was only observed at the highest concentration and there was no repeat of the experiment at the selected or other concentrations of the notified chemical. The notified chemical was not clastogenic in an in vivo micronucleus test in mice. Some cytotoxic effects were observed as determined by the decrease of the number of immature erythroblasts, indicating that the notified chemical has reached the bone marrow. Due to cytotoxicity of the notified chemical the test concentrations for all genotoxicity studies were low. The cytotoxicity of the notified chemical is most likely due to the surfactant characteristics and interference with the cell membrane. Based on the available data, the notified chemical is not considered mutagenic.

Health hazard classification
Based on the results of the eye irritation and skin irritation tests, the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrases:

R38 Irritating to skin
R41 Risk of serious damage to eyes

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
The notified chemical will be handled by workers at ≤87% concentration as imported, and at ≤15% in end-use products. Based on the available data, adverse effects associated with exposure to the notified chemical may include eye and skin irritation, with the greatest severity of effects expected to be associated with exposure to the raw material (≤87% notified chemical). The expected use of automated processes and PPE by workers should reduce dermal and ocular exposure levels and hence lower the risk of eye and skin irritation.

The notified chemical contains a low percentage (<9.6%) of respirable particles, hence a small portion of the notified chemical may reach the lower respiratory tract. At low concentrations this should be readily cleared from the lungs, unless high levels are inhaled. When high concentrations of the notified chemical are inhaled, it is likely to be cleared from the lungs, but this may be slower and temporary respiratory impairment is possible. There is no information on acute or chronic inhalation toxicity for the notified chemical. However, no systemic toxicity was observed in an acute oral toxicity study in rats or in repeat dose oral toxicity studies on the acceptable analogue Sodium Lauroyl Sarcosinate, indicating low toxicity of the notified chemical if absorbed. The expected use of suitable respirators and local exhaust ventilation when handling the powdered notified chemical by reformulation workers should reduce inhalation exposure levels and hence lower the risk of temporary lung overloading.

Provided that control measures are in place to minimise worker exposure, including the use of automated processes and PPE including respiratory protection where ventilation is inadequate when handling the powdered chemical, the risk to the health of workers from use of the notified chemical is not considered to be unacceptable.

The risk for beauty care professionals who regularly use products containing the notified chemical (up to 15%) is expected to be of a similar or lesser extent than that experienced by members of the public who use such products on a regular basis.

6.3.2. Public health
The public will have widespread dermal exposure to the notified chemical, which is proposed to be used at a level of up to 15% in rinse off and 5% in leave on cosmetic products. Ocular exposure is also a possibility due to accidental contact.

Eye contact with the notified chemical in rinse off products at concentrations of up to 10-15% may lead to serious eye damage. If the products were diluted with water when eye contact occurs, eye irritation may still occur, though the dilution and reduced contact time generally associated with use of rinse off products is expected to minimise this possibility.

When used in leave on products at concentrations up to 5%, the potential for eye irritation still exists. However, intentional ocular exposure is not expected, and rinsing of the eyes is recommended in the event of accidental exposure.

When using leave-on products, some skin irritation may occur, but is expected to be limited by the low proposed concentrations (up to 5%). Significant skin irritation effects are also not expected when rinse off products containing the notified chemical (up to 15%) are used due to dilution and the reduced skin contact time.

Though information was not available on the effects of long term repeated exposure to the notified chemical, information on sodium lauroyl sarcosinate suggests that the notified chemical is likely to be of low repeated dose toxicity.

In summary, use of products containing the notified chemical at concentrations up to 15% may lead to eye irritation. The risk is not expected to be significant when the notified chemical is present in rinse off products (up to 15%) due to the dilution and reduced skin/eye contact time. In addition, the risk of irritation effects due to the notified chemical in leave on products (up to 5%) is expected to be limited by the relatively low concentrations at which it is present. The eye and any possible skin irritation risk associated with use of the notified chemical in cosmetic products may be further minimised by the inclusion of appropriate labelling and directions for use to warn against eye contact and of the possibility of skin irritation reactions. Packaging directions, should recommend that use be discontinued if irritation occurs. When used in the proposed manner, with appropriate safety information on the packaging, the risk to the public associated with eye and skin contact with the notified chemical at the proposed concentrations is not considered to be unacceptable.

In addition, the risk associated with repeated exposure to the notified chemicals is not considered to be unacceptable.

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 finished cosmetic products and will also be imported as a raw material in aqueous solution or powdered form for blending. The notified chemical is expected to be released to landfill as residue remaining in containers (estimated to be up to 1% of the annual import volumes) and released to sewer from the cleaning of blending equipment (3%).

Accidental spills during transport or reformulation are expected to involve minimal amounts of the notified chemical and will be collected with inert material and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The majority of the notified chemical is expected to be washed to sewer as a result of its use pattern (as rinse-off and leave-on cosmetic products).

RELEASE OF CHEMICAL FROM DISPOSAL

Residue of the notified chemical in empty containers (1%) will share the fate of the container and will either be disposed of to landfill or washed to sewer when containers are rinsed before recycling. Waste and expired material is expected to be disposed of to landfill.

7.1.2 Environmental fate

The notified chemical is readily biodegradable and is expected to be largely degraded by sewage treatment processes. Approximately 33% of the total annual import of the notified chemical (calculated by SimpleTreat; European Commission, 2003) may be discharged to receiving waters in treated effluent as the notified chemical is water soluble, yet the notified chemical is expected to disperse and degrade. Bioaccumulation is not likely as the notified chemical is water soluble and readily biodegradable. In landfill, the notified chemical is expected to biodegrade to form water and oxides of carbon and nitrogen, and inorganic salts. For the details of the environmental fate studies refer to Appendix C.

7.1.3 Predicted Environmental Concentration (PEC)

The notified chemical was found to be readily biodegradable, thus, its removal from influent by sewage treatment plant (STP) processes is expected. A mitigated PEC is presented below, based on the assumption that all of notified chemical will be discharged to the aquatic compartment via STPs and taking into account degradation of up to 67% in STPs, as calculated by the SimpleTreat Model (European Commission, 2003):

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	45,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	45,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	123.29	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	21.161	million
Removal within STP	67%	
Daily effluent production:	4,232	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	9.61	µg/L
PEC - Ocean:	0.96	µg/L

7.2. Environmental effects assessment

The results from ecotoxicological investigations conducted on an analogue of the notified chemical (analogue 1) are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity (96 h)*	LC50 >100 mg/L	Not harmful
Aquatic Invertebrate Toxicity (48 h)	EC50 >80 mg/L	Not toxic
Algal Toxicity (72 h)	E_rC50 = 16.3 mg/L	Harmful

*Calculated by QSAR

Under the Globally Harmonised System of Classification and Labelling of Chemicals (United Nations, 2009) the notified chemical is classified as not harmful to fish, not toxic to aquatic invertebrates and harmful to algae. As the notified chemical is readily biodegradable, and it is not expected to bioaccumulate due to its water solubility, the notified chemical has not been classified for long-term effects.

7.2.1 Predicted No-Effect Concentration

The lowest endpoint from ecotoxicological studies on an analogue of the notified chemical was used to calculate the PNEC. Acute toxicity endpoints are available for the effects of the notified chemical on aquatic species from three trophic levels (two experimental results and one based on QSAR). An assessment factor of 500 was used since the QSAR result was not a conservative estimate.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
E_rC50 (algae)	16.3	mg/L
Assessment Factor	500	
PNEC:	32.6	µg/L

7.3. Environmental risk assessment

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q – River	9.61	32.6	0.295
Q – Ocean	0.96	32.6	0.029

The Risk Quotients (Q = PEC/PNEC) for the worst case discharge scenario have been calculated to be <1 for the river and ocean compartments. This indicates the notified chemical is not expected to pose an unacceptable risk to the aquatic environment based on its reported use pattern.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available data the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] with the following risk phrases:

R38 Irritating to skin
R41 Risk of serious damage to eyes

As a comparison only, the classification of notified chemical/polymer using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations, 2009) 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***
Skin irritation	2	Causes skin irritation
Irritant	2A	Causes serious eye irritation
Environment	Acute 3	Harmful 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 the proposed manner, the notified chemical is not considered to pose an unacceptable risk to public health.

Environmental risk assessment
The notified chemical is not expected to pose a risk to the environment based on its reported use pattern and estimated PEC/PNEC ratio.

Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- Safe Work Australia, should consider the following health hazard classification for the notified chemical:
  - Xi: R41 Risk of serious damage to eyes
  - Xi: R38 Irritating to skin

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - Conc. ≥20%: Xi; R41; R38;
  - ≥10% Conc. <20%: Xi; R41;
  - ≥5% Conc. <10%: Xi; R36.

- The notified chemical has previously been referred for scheduling in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) based on the results of skin and eye irritation tests.

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced and during reformulation into consumer products:
  - Adequate ventilation where exposure to dust or aerosols of the notified chemical is possible
  - Reformulation and packing conducted using enclosed and automated processes

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced and during reformulation into consumer products:
  - Avoid contact with skin and eyes
  - Avoid generation of dusts
  - Do not breathe dust
  - Provision of emergency eye wash facilities and showers

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced and during reformulation into cosmetic products:
  - Eye/face protection
  - Impermeable gloves
  - Coveralls
  - Suitable respirators where inhalation exposure to dusts of the notified chemical might occur.

  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 NOHSC *Approved Criteria for Classifying Hazardous Substances*, 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 at concentrations ≥5% should be labelled with a warning against eye contact, and directions on first aid measures if the product contacts the eye (e.g. avoid contact with eyes, in case of contact with eyes, rinse immediately with plenty of water and seek medical advice).

- Precautionary warning on possible skin irritation is also recommended for leave on products.

- The following measures should be taken to minimise public exposure to the notified chemical:
  - the notified chemical should not be used in spray products for consumer/domestic use.

Disposal

- The notified chemical should be disposed of to landfill.

Emergency procedures

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

Regulatory Obligations

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

Therefore, the Director 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 notified chemical is to be used in spray products.

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a component in leave-on (at ≤5%) or rinse-off (at ≤15%) cosmetic products, or is likely to change significantly;
- the amount of chemical being introduced has increased from 45 tonnes, or is likely to increase, significantly;
- if 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: PHYSICO-CHEMICAL PROPERTIES

Vapour Pressure Estimated $<10^{-5}$ kPa

Remarks The notified chemical is a solid with molecular weight of 279 Daltons and is estimated by the notifier to have a low vapour pressure of $<10^{-5}$ kPa.

Water Solubility <0.5% w/w at 25°C

Remarks A number of concentrations (0.5, 1, 2, 3, 5, 8, 10, 12, 15 and 18 wt.%) were prepared and dissolved in deionised water by heating at 80°C, and then cooled by air-cooling until their temperature reached 25°C. After 24 h, at 25°C, the state of each preparation was assessed visually. All samples were visually transparent in water at 80°C. Precipitation was observed after 24 h at 25°C in all samples. However, in promotional literature and some toxicological test reports it is stated that the 30% solution of the notified chemical was clear at 25°C. It is possible that this discrepancy is a result of the different solubility of the notified chemical and that of some impurities that could be present in the preparation tested for water solubility.

TEST FACILITY Not identified.

Dissociation Constant pKa = 4.64-5.86 (estimated)

Remarks The notified chemical is an anionic surfactant and would be expected to dissociate within the environmental pH range of 4-9. This is supported by the range of pKa values for some of the main chemical components of the notified chemical, namely Sodium Lauroyl Glycinate and Sodium Myristoyl Glycinate.

Particle Size

METHOD In house sieve method

Range (μm)	*Mass (%)*
<63	9.26
63-90	16.9
90-125	23.1
125-180	27.7
180-250	14.5
250-355	4.8
>355	0.33

Remarks D50 average 126 μm

TEST FACILITY Ajinomoto (2006)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified chemical

METHOD: In house method
- Species/Strain: Mice – ICR from Charles River Japan
- Vehicle: Water
- Remarks - Method: Ten 4-week old animals, 5/sex in each dose group, were used in each treatment dose group. They were dosed after 7 days of acclimatization period.
  Clinical symptoms were observed two and six hours following administration and once a day for the following 14days.
  Body weight was recorded at the time of dosing, and on the following days 1,7 and 14.
  All animals were sacrificed on day 14 and the organs were examined macroscopically.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	0	none
2	5/sex	1000	none
3	5/sex	2000	none

- LD50: >2000 mg/kg bw
- Signs of Toxicity: There were no deaths or significant test substance-related clinical signs and remarkable body weight changes during the study period.
- Effects in Organs: In autopsy a cyst in the left kidney in one case and an oedema in the uterus in one case was found in the female 1000 mg/kg group. Oedema in the left ovary was observed in one case in the female 2000mg/kg group. These conditions develop spontaneously in this type of mouse and they are not considered to be related to the administration of the test substance.
- Remarks - Results: Loss of vigour was observed in 1 male mouse in the 2000mg/kg group.
  Wet hair around the anus was observed during the observation period for one 1000mg/kg male, one 2000 mg/kg male and one 2000mg/kg female. No abnormality was observed and six hours and onwards and are probably related to the administration rather than the test article itself.

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

TEST FACILITY: Ajinomoto (1997a)

B.2. Irritation – skin

TEST SUBSTANCE: Notified chemical at 5%

METHOD: In house method scored by Draize scale analogous to OECD TG 404 Acute Dermal Irritation
- Species/Strain: Rabbit/New Zealand White Male
- Number of Animals: 6 treated and 12 controls (6 vehicle and 6 5% sodium lauryl sulphate as positive control)
- Vehicle: Water
- Observation Period: 7 days
- Type of Dressing: Occlusive for 24 hours
- Remarks - Method: Approximately 5% solution of the notified chemical was tested. The test concentration was chosen on the basis of the likely concentration of the notified chemical in final products. It was not stated whether the test

material was removed from the skin after the 24h test period.
The levels of erythema and oedema using Draize scale were evaluated after 30 min after patch removal (24 h post treatment) and 48h, 72h and seven days post treatment.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	1.83	3	≥72h to <1 week	0
Oedema	0	-	-	0

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

Remarks - Results

CONCLUSION The notified chemical is slightly irritating to the skin at concentrations of approximately 5% .

TEST FACILITY Ajinomoto (1998a)

B.3. Irritation – skin

TEST SUBSTANCE Analaogue chemical 1at 5% in aqueous solution

METHOD In-house modified Draize test
Species/Strain Rabbit/New Zealand White
Number of Animals 4 Males
Vehicle Distilled water
Observation Period 7 days
Type of Dressing Occlusive
Remarks - Method 0.3 ml of the test substance solution was placed on a patch with adhesive plaster and applied to previously clipped area of skin. The area was covered with a torso cover and left for 24 hours. Skin irritation was assessed according to the Draize scale at 24, 48 and 72 hours and 1 week after the application.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	1.08	2 (at 24 and 48 hr)	< 7 days	0
Oedema	0	0	0	0

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

Remarks - Results At the end of the observation period, all animals showed scaling of the skin. An erythema score of 2 (well defined erythema) was observed in 1 animal at 24 and 48 hours. This had reduced to score 1 (very slight erythema) by 72 hours. Erythema of score 1 was observed in the other 3 animals at 24 and 48 hours and remained at this level in 2 of the animals at 72 hours. Erythema resolved by day 7.

CONCLUSION The analogue chemical is slightly irritating to the skin at 5% concentration based on the erythema/eschar observed and the persistence of scaling in all animals up to day 7.

TEST FACILITY Ajinomoto Co Inc (1998c)

B.4. Irritation – skin

TEST SUBSTANCE	Analogue chemical 2; 30% purity Note: the concentration at which the chemical is present in the test substance is unclear from the test report.
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 males
Vehicle	None
Observation Period	14 days
Type of Dressing	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	1.7	1.0	2.7	4	14 days	4
Oedema	0	0	1.3	2	<72 hr	0

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

Remarks – Results	Slight oedema was observed in one of the animals at 24 and 48 hours after patch removal. Erythema was observed in all animals. In two of the animals the erythema was very slight to well-defined and had resolved by the 7 day observation, leaving scaling. It is unclear from the test report whether the scaling remained at the completion of the study. In the other animal, the erythema was well-defined at the 24 and 48 hour observation and then increased in severity to grade 4 (severe erythema (beet redness) to eschar formation preventing grading of erythema). The test report suggests that this was due to eschar formation. This persisted at the same severity at subsequent observations and remained at the final observation time (14 days).
CONCLUSION	The analogue chemical at the tested concentration is irritating to the skin based on the assumed persistence of scaling in two animals and erythema/eschar at the end of the observation period in the remaining animal.
TEST FACILITY	Ajinomoto Co Inc (2008a)

B.5. Irritation – eye

TEST SUBSTANCE	Notified chemical at 5%
METHOD	In house method scored by Draize scale analogous to OECD TG 405 Acute Eye Irritation
Species/Strain	Rabbit/New Zealand White Male
Number of Animals	6 treated and 12 controls (6 vehicle and 6 5% sodium lauryl sulphate as positive control)
Observation Period	7 days
Remarks - Method	Approximately 5% solution of the notified chemical was tested. The test concentration was chosen on the basis of the likely concentration of the notified chemical in final products. The cornea, iris, conjunctivae and discharge were evaluated using Draize scale at 24 h 48h, 72h, 96h and seven days post treatment.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	1.22	2	Present at 1 week	1
Conjunctiva: chemosis	0.78	2	48h	0
Conjunctiva: discharge	0.94	3	48h	0
Corneal opacity	1.17	2	96h	0
Iridial inflammation	0.06	1	24h	0

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

Remarks - Results: Effects on the conjunctivae had not resolved by the end of the observation period (7 days), which is a shorter period than the 21 days recommended in the OECD test method.

CONCLUSION: The notified chemical is irritating to the eye and causes persistent effects on the conjunctivae at concentrations of approximately 5%.

TEST FACILITY: Ajinomoto (1997b)

B.6. Irritation – eye

TEST SUBSTANCE: Analogue chemical 1at 1% and 5%, in aqueous solution.

METHOD: In-house modified Draize test
Species/Strain: Rabbit/New Zealand White
Number of Animals: 6 Males
Observation Period: 7 days
Remarks - Method: The observation period is 7 days, which is a shorter period than the 21 days recommended in the OECD test method. The report using 5% test substance did not provide individual scores for conjunctival symptoms at the 48 and 72 hour observation points, therefore the mean overall scores could not be calculated for conjunctival redness, chemosis and discharge. SLS (5%) was used as a positive control.

RESULTS

1% test substance

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	0.33	1	< 72 hours	0
Conjunctiva: chemosis	0	0	0	0
Conjunctiva: discharge	0	0	0	0
Corneal opacity	0	0	0	0
Iridial inflammation	0	0	0	0

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

5% test substance

Lesion	*Mean Score at 24 hours**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	2.83	3.0	Present after 7 days	1
Conjunctiva: chemosis	1.83	3.0	< 7 days	0
Conjunctiva: discharge	1.67	3.0	< 7 days	0
	*Mean Score^*			
Corneal opacity	0.08	1.0	< 48 hours	0
Iridial inflammation	0.33	1.0	< 48 hours	0

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

Remarks - Results: *1% test substance*: Only slight irritation effects observed at this concentration, which cleared within 72 hours.
5% test substance: Corneal opacity and iridial inflammation were only observed in one animal at the 24 hour observation. Conjunctival irritation

slowly improved over time. However, redness of the conjunctiva (score 1 – blood vessels normal) was still present after 7 days in four of the six animals.

CONCLUSION The analogue chemical is irritating to the eye at 5% concentration based on the persistence of irritation effects at the end of the 7 day observation period and mean conjunctival redness score of > 2.5 at 24 hours.

TEST FACILITY Ajinomoto Co Inc (1998d)

B.7. Irritation – eye

TEST SUBSTANCE Analogue chemical 2; 30% purity
Note: the concentration at which the notified chemical is present in the test substance is unclear from the test report.

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 1 male
Observation Period 10 days
Remarks – Method Only one animal was tested due to the severity of the effects observed in this animal.

RESULTS

Lesion	*Scores**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	2.66	3 (at 24, 48 hr)	< 10 days	0
Conjunctiva: chemosis	1.66	4 (at 1 hr)	< 96 hr	0
Conjunctiva: discharge	0	3 (at 5 min, 1hr)	< 24 hr	0
Cornea opacity	1.66	2 (up to 48 hr)	< 10 days	0
Iridial inflammation	0.66	1 (up to 48 hr)	< 72 hr	0

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

Remarks – Results The following observations were made of the treated eye.

- Corneal opacity with slightly obscured iris details, which persisted up until the 48 hour observation. After this the severity of the corneal opacity decreased and cleared by the 10 day observation.
- Iris congestion was observed but had resolved by 72 hours.
- Redness of the conjunctivae increased in severity with beefy red conjunctivae observed at the 24 and 48 hour observations. After this time the severity decreased and had cleared by the 10 day observation.
- Conjunctival swelling with about half or more of the eye lid closed was observed at the 5 minute and one hour time point. This decreased to obvious swelling at 24 and 48 hours and less again by 72 hours. By the 96 hour observation the chemosis had cleared.
- Considerable discharge from the eye was observed up to the 1 hour time point, after which it cleared.

CONCLUSION The analogue chemical at the tested concentration is irritating to the eye.

TEST FACILITY Ajinomoto Co Inc (2008b)

B.8. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD	Skin Sensitisation – Maximisation test
Species/Strain	Guinea pig/Hartley female
PRELIMINARY STUDY	Not performed
MAIN STUDY	
Number of Animals	Test Group: 10 Control Group: 5 Each testing material (notified chemical, vehicle and positive control were tested using 10 test and 5 control, saline-treated animals).
INDUCTION PHASE	Induction Concentration: intradermal: ~5% topical: ~5%
Signs of Irritation	Not recorded
CHALLENGE PHASE	16 days following intradermal and 10 days following topical induction
1st challenge	topical: ~5%
2nd challenge	Not performed
Remarks - Method	0.1% of 2,4-dinitrochlorobenzrne (DNCB) was used as a positive control. The skean was treated with sodium lauryl sulphate prior to dermal induction.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	~5%	0	0	-	-
Negative Control Group	~5%	0	0	-	-

Remarks - Results	Oedema and severe erythema were observed at 24 hours and 48 hours post challenge in all the animals in the Positive Control Test Group treated with DNCB.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test with approximately 5% of the notified chemical.
TEST FACILITY	Ajinomoto (1998b)

B.9. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	Study in compliance with Japanese regulatory standards for Microbial Mutagenicity and GLP standards. Pre incubation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	S9 fraction from Phenobarbital and 5,6-benzoflavone activated Sprague-Dawleyr Rat liver at 10%
Concentration Range in Main Test	Without metabolic activation for *S. typhimurium* strains: 2.4 to 78 µg/plate With metabolic activation for *S. typhimurium* strains: 10 to 313 µg/plate Without metabolic activation for *E. coli* strain 156 to 5000 µg/plate With metabolic activation for *E. coli* strain: 156 to 5000 µg/plate
Vehicle	Water (for the notified chemical)
Remarks - Method	Concentration of the tested material was 30% Appropriate vehicle and positive controls were used. The negative controls were within normal limits and the positive controls (2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide, sodium azide, 2-methoxy-6-chloro-9-[3-(2-chloroethyl) aminopropylamino] acridine.2HCl, 2-aminoanthracene,

Benzo(a)pyrene demonstrated the sensitivity of the test system.
The mutagenicity study on S. Typhimurium strains was repeated without metabolic activation because of growth inhibition in the initial test.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 78 for *S. typhimurium* 5000 for *E. coli*	78 for *S. typhimurium* 2500 for *E. coli*	Not observed	no
Test 2	-	78 for *S. typhimurium*	Not observed	no
Present				
Test 1	≥ 313 for *S. typhimurium* 5000 for *E. coli*	156 for *S. typhimurium* 2500 for *E. coli*	Not observed	no
Test 2	-	not performed	-	no

Remarks - Results: The observed cytotoxicity of the notified chemical at relatively low concentrations of the notified chemical is most likely due to the surfactant properties.

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

TEST FACILITY: BML (1997)

B.10. Genotoxicity – in vitro

TEST SUBSTANCE: Notified chemical

METHOD: Study in compliance with Japanese regulatory standards for Toxicity testing of Pharmaceutical products and GLP standards.

Species/Strain: Chinese hamster
Cell Type/Cell Line: Lung fibroblasts (CHL/IU) cells
Metabolic Activation System: S9 fraction from Phenobarbital and 5,6-benzoflavone activated Sprague-Dawleyr Rat liver at 5%
Vehicle: Saline
Remarks - Method: Concentration of the notified chemical in the test is stated to be ten times higher than in the table below. However, the dilution in the cell medium was not taken into account.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	4*; 8*; 12*; 16*	24h	24h
Test 2	4*; 8*; 12*; 16*	48h	48h
Test 3	7.8*; 15.6*; 31.3*; 62.5*	6h	24h
Present			
Test 3	7,8*; 15,6*; 31,3*; 62,5*	6h	24h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic	*Test Substance Concentration (µg/mL) Resulting in:*

Activation	*Cytotoxicity in Preliminary Test*	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	10.5	Not determined	Not observed	no
Test 2	-	16	Not observed	no[a]
Test 3				no
Present				
Test 1	42	-	-	-
Test 3	-	Not determined	Not observed	yes[b]

Remarks - Results

a There was a small increase of the percentage of cells with aberrations including gaps in cultures treated with 8 and 12 µg/mL of notified chemical (2% and 1.5%, respectively) compared with the solvent control (0%) . However, this is not considered to be significant as there were also some aberrant cells (0.5%) in the non-treated control while the positive control using treatment with MMC generated significantly higher increase. At the highest concentration tested in the Main test 1, the cytotoxicity was very high and did not allow for examination of sufficient number of cells to determine genotoxicity.

b The percentage of cells with aberrations including and excluding gaps was increased to 23% in the cultures treated with 62,5 µg/mL of notified chemical in the presence of metabolic activation. This increase was assessed as a positive genotoxic effect even though concentration dependent trend was not observed at the lower concentrations. In Tests 1 and 2, the incidence of structural aberrations was increased with the positive control Mitomycin C (MMC). In Test 3 the percentage of cells with structural aberrations tested with the positive control N-nitrosodimethylamine (DMN) i was increased in the presence of metabolic activation, but was not increased in the absence of metabolic .activation. A possible reason for the result is that this control requires metabolic activation.

CONCLUSION

The notified chemical was clastogenic to hamster lung fibroblasts (CHL/IU) treated in vitro in the presence of metabolic activation.

TEST FACILITY

BML (1998)

B.11. Genotoxicity – in vivo

TEST SUBSTANCE

Notified chemical

METHOD

In house method similar to OECD TG 474 Mammalian Erythrocyte Micronucleus Test.

Species/Strain: Mouse/ICR (Crj:CD-1) SPF

Route of Administration: Intraperitoneal twice within 24h

Vehicle: Saline

Remarks - Method: In a preliminary, range finding study, the LD50 for intraperitoneal administration was determined to be between 250 and 500 mg/kg bw.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	6 male	0	24h
II (low dose)	6 male	50	24h
III (mid dose 1)	6 male	100	24h
IV (mid dose 2)	6 male	200	24h
V (high dose)	6 male	400	24h
VI (positive control - M)	6 male	2	24h

M=mitomycin C

RESULTS

Doses Producing Toxicity	In the main test four deaths were observed in the 400 mg/kg bw group (4/6) and one death was observed in the 200 mg/kg bw group (1/6). A decrease in locomotor activity and bradypnea were observed in the 50mg/kg bw or higher concentration groups, piloerection was observed in the 100 mg/kg bw or higher concentration groups, hypothermia, lacrimation and prone position were observed in the 200 mg/kg bw or higher concentration groups.
Genotoxic Effects	None observed in the animals treated with the solvent control. No increase in the frequency of micronucleated polychromatic erythrocytes at any dose level or exposure time was observed in the dose range finding study or the main. The positive control showed a marked increase in the frequency of micronucleated polychromatic erythrocytes, indicating that the test system responded appropriately
Remarks - Results	The ratio of polychromatic erythrocytes to total erythrocytes was significantly decreased in the mid dose I (group III) and above. This finding suggests that the notified chemical has reached the bone marrow after intraperitoneal administration and it is toxic to erythroblasts.

CONCLUSION	The notified chemical was not clastogenic under the conditions of this in vivo Mammalian Erythrocyte Micronucleus Test.
TEST FACILITY	JBC (1998)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability (study 1)

TEST SUBSTANCE	Analogue of the notified chemical (Analogue 1; 30% aqueous solution)
METHOD	OECD TG 301 C Ready Biodegradability: Modified MITI Test (I).
Inoculum	Standard activated sludge (30 mg/L dry weight)
Exposure Period	28 Days
Auxiliary Solvent	None
Analytical Monitoring	Biological oxygen demand (BOD) and dissolved organic carbon (DOC) were determined using a Central Kagaku D unit BOD measuring apparatus and Shimadzu TOC-500 total organic carbon measuring apparatus, respectively.
Remarks - Method	The test was conducted according to the guidelines above at a test substance concentration of 340 mg/L. A non-culture vessel (containing test substance, at 340 mg/L, and deionised water) and reference control (aniline, 100 mg/L) were run in parallel. Test conditions: 25 ± 1°C, pH not reported. Biodegradability was calculated from the BOD data, corrected by an inoculum blank, and the theoretical oxygen demand (ThOD), assuming nitrification.

RESULTS

Test substance		*Aniline*	
Day	*% Degradation*	*Day*	*% Degradation*
7	65.8	7	56.7
14	73.2	14	63.6
21	75.2	21	66.2
28	79.8	28	69.5

Remarks - Results	Biodegradability of the test substance after 28 days was 79.8%, and reached >60% in a 10-day window. Oxygen consumption of the reference material in the control was >40% after 7 days, and 63.6% after 14 days. A test is considered valid if consumption is >40% after 7 days, and >65% after 14 days. Although the Day 14 result is slightly lower than 65%, it is not expected to affect the result of the test substance. Biodegradability of the test substance based on DOC was >90% after 28 days. Degradation also occurred in the non-culture vessel, reaching 43% after 28 days based on BOD.
CONCLUSION	The test substance, and by inference the notified chemical, can be classed as readily biodegradable.
TEST FACILITY	Japan Food Research Laboratory (1995)

C.1.2. Ready biodegradability (study 2)

TEST SUBSTANCE	Notified chemical
METHOD	The study was conducted in accordance with the Test Method Relating New Chemical Substances (Kanpogyo No. 5, Yakuhatsu No. 615, 49 Kikyoku No. 392, 1974), which prescribes the procedure for testing new chemical substances as required by the Chemical Substances Control Law of Japan.
Inoculum	1) Mixed liquor suspended solid (MLSS): 5500 mg/L 2) Source: Chemical Biotesting Center, Chemical Inspection and Testing Institute, Japan

	3) Date of receipt: October 22, 1998
Exposure Period	28 days
Auxiliary Solvent	
Analytical Monitoring	Determination of test substance by HPLC
Remarks – Method	Study concentration of test substance 100 mg/L and reference substance Aniline) 100 mg/L.

RESULTS

Test substance- Potassium Cocoyl Glycinate		Reference Substance- Aniline	
Day	*% degradation **	*Day*	*% degradation*
7	72.6	7	67
14	78.0	14	73
21	79.7	21	74
28	80.3	28	75

*Average of three tests

Remarks – Results	The 28 day individual results for the three tests were 78%, 78% and 85%. The average was 80.3%

CONCLUSION The notified chemical, can be classed as readily biodegradable.

TEST FACILITY Yokohama Laboratory (1999)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE Notified chemical

METHOD QSAR estimation methods

RESULTS

ECOSAR (v1.00) *Anionic surfactant class* *LC50 (96 h) mg/L*
> 100

REMARKS - RESULTS

Surfactant toxicity has been found to depend on carbon chain length (Nabholz et al., 1993) and consequently, QSARs based on chain length have been derived and validated for fish (US EPA, 2009). If the toxicity of a mixture is to be estimated, usually the weighted average carbon chain length (WACCL) is used for the calculation. In the notified chemical the cocoyl acid profile depends on the source coconuts and, as a result, the WACCL is variable. The chain length of the most abundant component is C12 (i.e. the lauroyl derivatives). However, since the hydrophobic side chain of the notified chemical is complex (i.e. not a straight chain alkyl group) the Kow of the side chain was calculated and the alkyl side chain with the closest Kow (C8) was used for the estimation of fish toxicity (method suggested by Clements et al., 1996). This gave an endpoint of LC50 (96 h) > 100 mg/L (US EPA 2009, ECOSAR (v1.00), anionic surfactant class).

CONCLUSION The notified chemical is not harmful to fish

TEST FACILITY US EPA (2009)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Analogue of the notified chemical (Analogue 1)

METHOD OECD TG 202 *Daphnia* sp. Acute Immobilisation Test – Static.
Species *Ceriodaphnia dubia*
Exposure Period 48 hours
Auxiliary Solvent None
Water Hardness 91 mg $CaCO_3$/L
Analytical Monitoring None
Remarks - Method The test was conducted according to the guidelines above at test substance concentrations of 80.0, 40.0, 19.7, 10.0 and 5.1 mg/L. The test substance did not completely dissolve upon addition of dilution water. The solutions were stirred for 24 h, and allowed to settle for 5.5 h. All solutions were observed to contain suspended material, and the 80 mg/L solution contained precipitate on the bottom of the vessel. The solutions were siphoned off into clean vessels to remove the suspended matter. A control and toxicant reference control were run in parallel. Test conditions: 25 ± 1°C, 16 h/8 h light dark cycle, pH 7.9–8.2, 97.4–100.4 mg O_2/L.

RESULTS

Concentration mg/L		*Number of C. dubia*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	Not tested	20	0	0
5.1	Not tested	20	0	0
10.0	Not tested	20	0	0
19.7	Not tested	20	0	0
40.0	Not tested	20	0	2
80.0	Not tested	20	0	6

EC50 >80 mg/L at 48 hours
NOEC 40 mg/L at 48 hours
Remarks - Results After siphoning, all the solutions still contained suspended material. The 80.0 mg/L solution was also cloudy in appearance. There were no immobilised daphnia in the control after 48 h, and the reference toxicant endpoint was between the acceptable limits 179.1–268.7 mg KCl/L (260.8 mg KCl/L), thus validating the test.

CONCLUSION The test substance, and by inference the notified chemical, is not toxic to aquatic invertebrates

TEST FACILITY Ecotox (2009)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE Analogue of the notified chemical (Analogue 1)

METHOD OECD TG 201 Alga, Growth Inhibition Test.
Species *Pseudokirchneriella subcaptiata*
Exposure Period 72 hours
Concentration Range Nominal: 0–32.0 mg/L
Actual: Not reported
Auxiliary Solvent None
Water Hardness Not reported
Analytical Monitoring A spectrophotometer was used to measure algal density
Remarks - Method The test was conducted according to the guidelines above at test substance concentrations of 32.0, 15.9, 8.0, 4.4, 2.4, 1.2, and 0.6 mg/L in triplicate. A blank and reference toxicant control (potassium chloride) were run in parallel. Test conditions: 25 ± 2°C, pH 7.7–8.9, continuous illumination. The endpoints and confidence limits were determined by linear interpolation, and Dunnett's Test (Toxcalc v5.0.31).

RESULTS

Biomass		*Growth*	
E_bC_{50} *mg/L at 72 h*	*NOEC* *mg/L*	*E_rC_{50}* *mg/L at 72 h*	*NOEC* *mg/L*
5.7 (4.3–6.4)	1.2	16.3 (14.5–18.3)	1.2

Remarks - Results	After mixing, all solutions contained a small amount of suspended matter, and the 32.0 mg/L solution appeared cloudy. Negative inhibition (i.e. stimulation) was observed for the test substance at concentration 1.2 mg/L at 72 hours. Cell density of the control increased 195-fold, and the reference toxicant endpoint was between the acceptable limits 0.9–4.2 g KCl/L (2.6 g KCl/L), thus validating the test.
CONCLUSION	The test substance, and by inference the notified chemical, is harmful to algae
TEST FACILITY	Ecotox (2009)

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