File No: EX/78(LTD/1124)

December 2005

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Glycine, N-(1-oxooctyl)-

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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
Chemicals Notification and Assessment

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FULL PUBLIC REPORT

Glycine, N-(1-oxooctyl)-

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Holder of the original assessment certificate (No. 1781, LTD/1124):
Johnson & Johnson Pacific Pty Ltd (ABN 73 001 121 446)
Level 3, 1 Bay Street
Broadway NSW 2007

Applicant for an extension of the original assessment certificate:
Bronson and Jacobs Pty Ltd (ABN: 81 000 063 249)
Australia Centre
5 Parkview Dr
Olympic Park NSW 2127

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

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

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

CHEMICAL NAME
Glycine, N-(1-oxooctyl)-

OTHER NAME(S)
Capyloyl Glycine

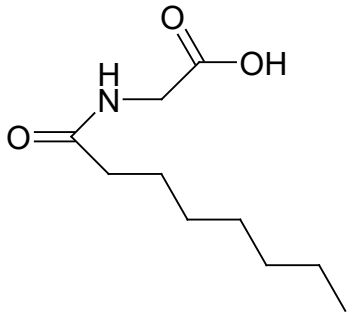
MARKETING NAME(S)
Lipacide C8G
Component of Sepicontrol A5
Component of NEUTROGENA SKINCLEARING® Gel

CAS NUMBER
14246-53-8

MOLECULAR FORMULA
$C_{10}H_{19}NO_3$

MOLECULAR WEIGHT
201.37

STRUCTURAL FORMULA



SPECTRAL DATA

ANALYTICAL METHOD	IR film between NaCl plates range 4000cm-1 to 600cm-1
Remarks:	The IR Spectrum has major peaks at 3312, 2924, 2850, 1698, 1547, 1466, 1413, 1337, 1277, 1234, 1206, 1038, 945, and 679 cm^{-1}
TEST FACILITY	Societe d'Exploitation des Produits Pour l'Industrie Chimique S.A. (SEPPIC S.A.), 75 quai d'Orsay- 75521 Paris Cedex 07- France

3. COMPOSITION

DEGREE OF PURITY
>98%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (>1% by weight)
None

ADDITIVES/ADJUVANTS
None

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported into Australia as a raw material for use as a cosmetic raw material and as a component of finished personal care products at a maximum concentration of 2%. The notified chemical will not be made in Australia.

Maximum Introduction Volume of Notified Chemical (100%) Over Next 5 Years

Year	*1*	*2*	*3*	*4*	*5*
	Tonnes	*Tonnes*	*Tonnes*	*Tonnes*	*Tonnes*
Johnson & Johnson Pacific Pty Ltd	0.25	0.25	0.25	0.25	0.25
Bronson and Jacobs Pty Ltd	0.5	0.5	0.5	0.5	0.5

USE
Used at levels of up to 2% as an emulsifier and a skin and hair conditioning ingredient and as a component of facial gels.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
The notified chemical will initially be imported as the notified chemical itself through Sydney and Melbourne by wharf and for the end use products through Sydney.

IDENTITY OF MANUFACTURER/RECIPIENTS
Johnson & Johnson Pacific Pty Ltd (ABN 73 001 121 446)
Level 3, 1 Bay Street
Broadway NSW 2007.

The identity of local manufacturers wishing to use a commercial raw material containing the notified chemical is unknown until the raw material is available for import and sale.

TRANSPORTATION AND PACKAGING
The notified chemical will be imported as a component of finished personal care products in 15 mL plastic tubes packed in individual consumer packaging. The individual packages are shrink wrapped and packaged into a carton. The products will be stored at the notifier's contract warehouse prior to transportation by road to the distribution warehouses for retail outlets, who will supply the products to retail outlets for consumer use.

The notified chemical will be imported as a commercial raw material in 20 kg drums on pallets inside containers and will travel from the wharf by road transport to the Orica Limited, Warehouse and Distribution Centre, 215 Dohertys Rd, Laverton, North Victoria 3026. It will be transported to manufacturing companies still unknown by road transport.

STORAGE FACILITIES & STORAGE REQUIREMENTS
The drums and cartons on pallets will be stored in a racked warehouse. The warehouse is fully bunded so that any spills can be directed to waste water pits on each site. No national or industry codes of practice or guidance notes or Australian Standards are applicable to the storage of this raw material.

5.2. Operation Description

The ready to use personal care product to be imported will be distributed to retail outlets to be used as facial gels.

For production of personal care products, a compounder will weigh an appropriate amount of the undiluted notified chemical into a separate container then add the amount directly into the mixing tank. In the mixing vessel heating will be required to melt the commercial raw material.

The Chemist samples the tank contents using a dip tube (large pipette) and tests the ingredient for QA purposes.

Packers monitor the line filler and the capper where the finished product is filled into retail bottles.

Store Persons remove the pallets of finished product from the end of the packing line and store the finished product in the finished store. They also receive the ingredient when first delivered and store it in the raw material store. Quantities of the ingredient would be issued to the Compounder for production as required.

5.3. Occupational exposure

For the imported facial gels, warehouse workers will handle products containing the notified chemical while contained in their outer carton. Retail workers will handle the products in their retail packaging. Worker exposure to the notified chemical may occur during transport and storage of the product containing up to 2% of the notified chemical if the packaging is breached.

For the compounded personal care products approximately 10 dockside and ware house workers per shipment will be involved in transporting the notified chemical from the wharf to the Company sites and placing the pallets of product into their warehouses. Dockside and warehouse workers may handle

monthly shipments for 4 hours per day.

A further two warehouse workers in the end user's warehouse will be involved in transferring pallets from the warehouse to the retailer's central distribution depots.

Dockside and warehouse workers routinely wear uniforms and safety shoes. They are not expected to have any contact with the notified chemical, except in the case of spills.

Mixing and dispensing will be carried out in a closed system or in one designed not to create aerosols or a dust hazard. During the weighing and transfer process, the compounder may be exposed to drips, spills and vapours. The compounder is to wear safety glasses with shields, gloves, apron or coverall, however respiratory protection is not required as there would be plenty of general ventilation.

The QA Chemist wears equipment to protect eyes, and skin, both body and hands.

Packers wear safety glasses and gloves for skin, body and hand protection.

OCCUPATIONAL HEALTH MONITORING (BIOLOGICAL MONITORING & ATMOSPHERIC MONITORING)
The inhalation exposure for a compounder is not known but expected to be low as the commercial raw material is a solid melting at 105°C. Inhalation exposure of the notified chemical during blending with heating is not expected as the blending process is automated and occurs in a closed vessel. No atmospheric monitoring is therefore proposed.

The dermal exposure will be accidental (gloves are normally worn) and is calculated to be 0-0.1mg/cm^2/day. Both hands can be exposed which corresponds to an exposed dermal area of 840cm^2. The assessed dermal exposure is 0-84 mg/day or 0-1.2mg/day/kg bw for a 70 kg worker. Limited biological monitoring will be ongoing by exception with clinical observation for skin or eye irritation as the most practical measure of monitoring workers.

Evidence of environmental contamination may be obtained using absorbent materials to mop exposed surfaces and HPLC analyses for the chemical. Since the chemical will be handled, mixed and dispersed in closed systems and at low usage rates, environmental contamination is likely to be very low or non-existent under normal working conditions.

5.4. Release

RELEASE OF CHEMICAL AT SITE
For production of personal care products release to the environment may be considered at several stages:

- Transport of the chemical prior to formulation. This is not likely to constitute a major hazard, as the material is likely to be containerised, or in packaging designed to withstand impact.

- Storage and product formulation. With the relatively low level use proposed for this product, with its formulation and dispensing in closed systems, it is unlikely that there will be any significant release to the environment.

In a formulated product the process is a batch process with a batch typically 6 tonne with each batch containing 120 kg of the notified chemical being produced in 4 hours, 4 batches per year. Emissions to waste water are possible while cleaning the equipment. It is estimated that 2-3% final product are rinsed into the waste water collection which then goes to a biological treatment plant. The content emitted is 500 kg x 3%/ 365 = 0.04 kg per day over a period of 1 year.

RELEASE OF CHEMICAL FROM USE
From importation of the notified chemical into Australia as a component of facial gels, the main source or release will be to sewer following washing after application. Some residual product will be retained in packaging, and will go into domestic rubbish and ultimately into landfill. This is not expected to exceed more than 1% of the import volume, and disposal will be dispersed around the country.

Given the use pattern of the notified chemical following compounding, initial release is entirely expected to occur to the aquatic compartment. Assuming the maximum importation volume of 500 kg of notified chemical and use the notified chemical occurring all year, the average daily release is expected to be 1.37 kg.

5.5. Disposal

Waste and expired material is expected to be disposed of according to Federal, State and Local government regulations.

If a spill occurs the spill is to be shovelled up or absorbed with sand or other absorbent and the area washed with water. Solutions are neutral pH. The chemical is biodegradable. It is to be disposed of to approved landfills. If the product is burnt the combustion products will be carbon oxides and nitrogen oxides.

5.6. Public exposure

When the notified chemical is imported as a component of facial gels public exposure during transport and storage is unlikely unless the packaging is breached. Public exposure will result through use of the facial gels containing a maximum of 2% notified chemical. Consumers will apply the product on the face twice daily. The average quantity of the product used per application is 0.8 grams (0.016 grams notified chemical/application or 0.032 grams notified chemical/day).

When the notified chemical is imported for compounding into personal care products public exposure to the notified chemical (in products) as a result of transportation within Australia is unlikely unless there is an accident. The material safety data sheets (MSDS) supplied for the commercial product have adequate instructions for clean-up and disposal of any accidental spills and therefore public exposure as a result of a transport accident is likely to be negligible.

If the notified chemical is blended in Australia to produce finished cosmetic creams or lotions or hair products then direct public exposure as a result of blending to the notified chemical is considered to be negligible since adequate engineering controls and standard operating procedures largely prevent any significant release of the notified chemical into the immediate vicinity of the site of blending.

Since the finished products will be sold to the general public, widespread public exposure is expected. Members of the public are likely to make dermal and possibly ocular contact with the notified chemical as a result of use of the product at a concentration of 2.00%. Since the finished products will be stored and used in a domestic environment, there is the possibility of accidental ingestion by a child. Because the notified chemical is of low acute oral toxicity, no adverse effects are expected as a result of ingestion of the notified chemical in the product.

The notified chemical may be released into the environment as a result of disposal of waste from blending, accidental spills during transport or disposal of diluted products and containers after use. The environmental releases are expected to be relatively small and most of the notified chemical released into the environment is expected to enter sewers where large dilutions are expected. Therefore, environmental concentrations are expected to be very low.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa White crystalline powder

Melting Point/Freezing Point 105°C

METHOD OECD TG 102 Melting Point/Melting Range.
EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
SEPPIC Method S52009B

Remarks The melting point was determined in duplicate using Differential Scanning Calorimetry.

TEST FACILITY University Analytical Laboratory, UNSW (2003)
Societe d'Exploitation des Produits Pour l'Industrie Chimique S.A. (SEPPIC S.A.), 75 quai d'Orsay- 75521 Paris Cedex 07- France.

Boiling Point Not determined

Remarks The material decomposes at temperatures between 206 to 208°C

Density 501 kg/m^3

METHOD OECD TG 109 Density of Liquids and Solids.
EC Directive 92/69/EEC A.3 Relative Density.

Remarks The density of the powder was determined using the Air Comparison Pycnometer method.

TEST FACILITY University Analytical Laboratory, UNSW (2003)
Societe d'Exploitation des Produits Pour l'Industrie Chimique S.A. (SEPPIC S.A.), 75 quai d'Orsay- 75521 Paris Cedex 07- France

Vapour Pressure Not determined

Remarks The notified chemical is not expected to have a significant degree of volatility. QSAR calculations using the EPA MPBPWIN v1.40 program gave values between 1.1×10^{-7} kPa and 4.1×10^{-7} kPa indicating slight volatility.

Water Solubility 2.8 g/L at 20°C

METHOD OECD TG 105 Water Solubility.

Remarks The water solubility was determined using the flask method at 20^{0}C. The test compound was dissolved in a known amount of water over a three-day period, centrifuged, and an aliquot of the supernatant evaporated and dried until a constant weight was achieved. Values for days 1, 2 and 3 were 2.77, 2.81 and 2.90 g/L respectively. The chemical can be considered readily soluble.

TEST FACILITY University Analytical Laboratory, UNSW (2003)
Societe d'Exploitation des Produits Pour l'Industrie Chimique S.A. (SEPPIC S.A.), 75 quai d'Orsay- 75521 Paris Cedex 07- France

Hydrolysis as a Function of pH

METHOD OECD TG 111 Hydrolysis as a Function of pH.

pH	*T (°C)*	*Mean loss (%)*
4	50/20	11.1/8.5
7	50/20	1.4/10.7
9	50/20	1.5/4.1(gain)

Remarks The test was conducted over 5 days at 20 and 50°C. Concentrations were analysed by HPLC. The results for 20°C were not used because crystals were observed in the buffering solution and it is possible that the buffering salts may have salted out the test material at this temperature. At 50°C, losses after five days suggest that

hydrolysis will not be a major removal process, with a half-life in the order of months under ambient conditions.

TEST FACILITY University Analytical Laboratory, UNSW (2003)

Partition Coefficient (n-octanol/water) log Pow at 20°C = 1.24

METHOD OECD TG 107 Partition Coefficient (n-octanol/water), Shake Flask Method.

Remarks Analytical Method: The concentration of the notified chemical in the aqueous layer and the octanol layer was determined by HPLC. The mean Pow was based on 6 samples with a range of Pow = 17.00-17.48 (LogPow range of 1.23-1.24)

TEST FACILITY University Analytical Laboratory, UNSW (2003)

Adsorption/Desorption Not determined

Remarks The low Log Kow indicates partitioning to organic carbon will also be low. A Log Koc value of 1.48 has been derived through modelling (PCKOCWIN v1.66).

Dissociation Constant Not determined.

Remarks The notified chemical has a free carboxylic acid group; the pK_a is expected to be around 2.34 (based on glycine) [Merck Index, 2001]. This indicates the chemical may be ionised throughout the environmentally relevant pH range of 4-9.

Particle Size 42.0 microns

METHOD Coulter® LS Particle Size Analyzer.

Range (μm)	*Mass (% cumulative)*
<10.4	10
<21.8	25
<39.2	50
<58.2	75
<76.6	90

Remarks The particle size distribution was determined after dispersing the sample in cyclohexane. The particle size ranged from 1.7 μm to 170 μm with a mean particle size of 42 μm.

TEST FACILITY University Analytical Laboratory, UNSW (2003)

Flash Point >100°C at 101.3 kPa

METHOD AFNOR Method No NFT60103

TEST FACILITY Societe d'Exploitation des Produits Pour l'Industrie Chimique S.A. (SEPPIC S.A.), 75 quai d'Orsay- 75521 Paris Cedex 07- France

Flammability Limits Not determined

Remarks The product in which the notified chemical is to be introduced is non-combustible.

Autoignition Temperature Not determined

Remarks The product in which the notified chemical is to be introduced is non-combustible.

Explosive Properties Not determined

Remarks The notified chemical is not expected to present an explosive hazard.

Reactivity

Remarks The notified chemical is expected to be stable under normal conditions of use.

7. TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion*
Rat, sub acute oral LD50 >10000 mg/kg bw	low toxicity
Skin Irritation - Chorio-allantoic Membrane (1% notified chemical)	non-irritating
Skin Irritation – Red Blood Cells (10% notified chemical)	non-irritating
Skin irritation, Guinea pigs, 14-day repeat application (5% notified chemical)	non-irritating
Human, skin irritation (1.6% notified chemical)	slightly irritating
Human, skin irritation (2% notified chemical)	slightly irritating
Eye irritation – Rabbits (5% notified chemical)	non-irritating
Skin sensitisation – Guinea pigs, adjuvant test (notified chemical powder)	non-sensitising
Skin sensitisation – Guinea pigs, adjuvant test (notified chemical powder)	non-sensitising
Human, skin irritation and sensitisation (5% notified chemical)	slightly irritating and no evidence of sensitisation
Human, skin sensitisation (1.6% notified chemical)	inadequate evidence of sensitisation
Genotoxicity – bacteria (notified chemical)	non-genotoxic

7.1. Subacute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	The method used is an in-house test method consisting of 10-day repeat dose study with limited observations similar to OECD TG 401 Acute Oral Toxicity.
Species/Strain	Rat/Sprague Dawley
Vehicle	Gum Arabic
Remarks - Method	The notified chemical was administered orally for 10 consecutive days as a 5% suspension in gum Arabic. Animal observation was conducted for 15 days after the last treatment. On day 15, autopsies were performed on the decedents and microscopic examinations on the organs of the abdomen and thorax were conducted on the survivors.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I (Low dose)	10/sex	2500	3
II (Mid dose)	10/sex	5000	2
III (High dose)	10/sex	10000	2

LD50	>10000 mg/kg bw
Signs of Toxicity	Three animals died between 6 to 15 days after administration of low dose and two animals died between 6 to 14 days after administration of mid and high dose. Weight reduction was observed in all dose groups. The weight reduction was not significant compared with control group and the animals seemed to recover towards the end of the observation period, except for males in mid dose group. Males in the mid dose group had lower weights compared with the control group and the weight reduction was observed throughout the treatment period. Decrease in food consumption in all groups at the end of treatment period was also observed.
Effects in Organs	The autopsy revealed thinning of the stomach wall in one animal at low

	dose and a dilated abdomen full of pus in another animal at mid dose group. No evidence of lesions was observed in high dose group. No microscopic observations were reported at necropsy.
Remarks - Results	The decrease in food consumption observed in all dose groups is reported to be due to overload of product in the intestines, which could also be the cause of observed weight loss.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Department Recherche et Essais Biologiques Stallergenes (1979)

7.2. Skin Irritation - Chorio-allantoic Membrane In vitro Screening

TEST SUBSTANCE	Notified chemical
METHOD	HET-CAM Test on the Chorio-allantoic Membrane of Fertilised Leghorn Hens' Eggs
Remarks - Method	The test was stated to be carried out based on the official method published on 26 December 1996, Appendix IV – Internal Procedure 57CO009
RESULTS	
Remarks - Results	There was no vasodilation observed from the new capillaries or dilation of capillaries, which were already visible. The score obtained was zero, which indicates that the notified chemical was a non-irritant. A summary only was provided. Scores for haemorrhage and coagulation were also zero.
CONCLUSION	The notified chemical was considered non-irritant at 1% concentration under the conditions of the test.
TEST FACILITY	Roso and Amalric (1999)

7.3. Skin Irritation – Red Blood Cell In vitro Screening

TEST SUBSTANCE	Notified chemical
METHOD	RBCA Test on Red Blood Cells
Remarks - Method	The test was stated to be carried out according to a method adapted from INVITTOX Protocol No: 37. A summary only was provided.
RESULTS	
Remarks - Results	The notified chemical did not show a hemolysing and denaturing properties when tested with red blood cells.
CONCLUSION	The notified chemical was considered non-irritant at 10% concentration under the conditions of the test.
TEST FACILITY	Roso and Guichard (2001)

7.4. Skin Irritation – Guinea pigs, repeat application

TEST SUBSTANCE	Lipacide C8G (5% Active Ingredient) Aqueous Dispersion
METHOD	Japanese MHW Guidelines, 1998.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3/sex
Vehicle	Water.
Observation Period	14 days.

Type of Dressing	Non-occlusive.
Remarks - Method	Fourteen non-occluded consecutive samples of 0.05 mL was applied over 14 days at 24-hour intervals. Immediately before each daily application and approximately 24 hours after the 14th application, the test sites were examined for evidence of primary irritation.

RESULTS

	No signs of skin irritation, no abnormal clinical signs and no abnormal body weight changes compared to controls were noted during the observation period.
Remarks - Results	None.

CONCLUSION	The notified chemical (5%) is non-irritating to the skin when administered repeatedly for 14 days.
TEST FACILITY	Safepharm Laboratories (1999a).

7.5. Skin irritation – human volunteers

7.5.1. Single patch test – 5% notified chemical

TEST SUBSTANCE	Test substance containing 5% of the notified chemical.

METHOD

Study Design	Single Patch Test
Study Group	10 female; age range 19 - 57
Vehicle	Distilled water
Procedure	The test substance was applied on the back of the subjects under an occlusive patch for 48 hours. A negative control containing water was performed under the same conditions. Cutaneous macroscopic examinations were performed about 30 minutes after removal of the patches and the reactions were scored.
Remarks - Method	All subjects completed the study.

RESULTS

Remarks - Results	Neither significant cutaneous intolerance nor a reaction of pathological irritation was observed. Three subjects had very slight erythema (hardly visible).

CONCLUSION	The test substance containing 5% of the notified chemical is slightly irritating.
TEST FACILITY	Institut d'Expertise Clinique (1996)

7.5.2. 6 application repeat patch test – 1.6% notified chemical

TEST SUBSTANCE	Gel containing 1.6% of the notified chemical.
METHOD	The test was in accordance with Johnson and Johnson Consumer Products Worldwide Protocol Nos: 28252.05, 28269.05, 28271.15, 28150.05, 28151.15 and 28151.05C and the Informed Consent conforms with 21 CFR 50.25: Protection of Human Subjects.
Study Design	Cumulative Irritation Test
Study Group	32 subjects (10 male, 22 female, age range 20 – 68); 29 completed the study.

Procedure	The exposure treatment consisted of a total of 6 applications of the test substance on the back of each subject under semi-occlusive conditions for 48 hours (72 hours on the weekend) over a 14-day period. At the removal of each patch, the test site was evaluated and an identical patch applied to the same site.
Challenge Procedure	The gel containing 1.6% of the notified chemical exhibited slight irritation potential in the 29 subjects tested (total score of 48 out of a potential maximum score of 724).
Remarks - Method	Three subjects did not complete the study. None of these subjects discontinued due to test material reaction.

RESULTS

Remarks - Results	Dryness and low-level, transient reactions were observed during the study. Distinct erythema (graded as 1) was observed at some stage in six out of twenty nine subjects.

CONCLUSION	The gel containing 1.6% of the notified chemical is not expected to cause irritation under conditions of normal use.
TEST FACILITY	Harrison Research Laboratories (2003a)

7.5.3. 21 day product trial – 2% notified chemical

TEST SUBSTANCE	Lotion containing 2% of the notified chemical.
METHOD	The test was in accordance with "Bonnes Pratiques Cliniques" by the Ministry of Employment and Population Affairs and the Ministry of Public Health and Family Affairs in France.
Study Design	The cutaneous tolerance of the product was assessed after clinical examination and questioning of the volunteers. The cosmetic qualities and acceptability were appreciated by means of a questionnaire at the end of the study. The sample given to volunteers was weighed before and after the study to calculate the average consumption of the product per volunteer for the test period. No application of any similar product to the tested one was allowed during the test period.
Study Group	20 female subjects, age range 20 – 65; 19 completed the study.
Procedure	After removal of make up with the usual cleansing milk, the volunteers were asked to apply the product to face by means of cotton wool at least twice a day for 21 (±1) days. The examinations were conducted before the first application of the product (Day 0) and at the end of the study (Day 22). After each examination, the volunteers were questioned about cutaneous reactions and any sensations of discomfort felt during the study. For the assessment of the cosmetic qualities and acceptability, the volunteers were asked to include any observations felt in the product evaluation sheet. At the end of the study, the volunteers were asked to complete a questionnaire.
Remarks - Method	Two subjects broke the container of the product and 1 subject did not bring back the flask at the end of the study.

RESULTS

Remarks - Results	On Day 0, cutaneous disorders in four volunteers compatible with the inclusion criteria were observed. There was no sign of cutaneous intolerance observed at the end of the study. Six volunteers reported sensations of discomfort, such as drying up, pulling, stinging or casual

redness (in 2 cases). Although these effects were treatment related, it was also reported that such effects could have been due to an insufficient moisturising power.

CONCLUSION The lotion containing 2% of the notified chemical is well tolerated by the skin and the cosmetic qualities and acceptability were well appreciated by the volunteers.

TEST FACILITY EVIC CEBA (1996)

7.6. Skin irritation and sensitisation– human volunteers

7.6.1. 9 application repeat insult patch test – 5% notified chemical

TEST SUBSTANCE Test substance containing 5% of the notified chemical.

METHOD Method of Marzulli and Maibach (Marzulli and Maibach, 1976)

Study Design	A preliminary study was conducted to determine the highest concentration not causing primary and cumulative irritation reactions. Based on the results from the preliminary study, the main study was conducted to investigate the irritation and sensitising potential of the notified chemical.
Study Group	Preliminary Study: 10 volunteers (9 females and 1 male; age range 21 – 63); Main Study: 50 volunteers (45 females and 5 males; age range 19 – 59)
Vehicle	Distilled water
Preliminary Study	Four successive applications (48 or 72 hrs) of three concentrations (1, 2.5 and 5%) were made under occlusive conditions.
Induction Procedure	The induction phase consisted of 9 consecutive patch applications of the test substance in occlusive conditions for 48 or 24 (4^{th} application), or 72 hours for the first 2-week ends, to the skin of the arm. Skin reactions were observed (macroscopically) after removal of each patch.
Rest Period	15 days
Challenge Procedure	A single patch was applied to a site previously unexposed to the test subject (to the skin of the back). The patch was removed after 48 hours and the site graded. The sites were graded (macroscopically) at 24 and 48 hours after removal of the patch.
Remarks - Method	One subject discontinued during the induction period and another subject during the rest period. No subjects discontinued due to test material reaction.

RESULTS

Remarks - Results	The maximum non-irritant concentration in the preliminary test was found to be 5%, the highest concentration used. In the main study, the majority of the subjects had minor transient irritation reaction. A single subject had a cumulative score (sum of irritation scores on a 0-4 scale over eight observations) of greater than 2. Neither pathological irritation, nor sensitisation reaction significant of a cutaneous intolerance was noted.

CONCLUSION The test substance containing 5% of the notified chemical is slightly irritating and there was no evidence of sensitisation reaction under the experimental conditions used.

TEST FACILITY Institut d'Expertise Clinique (1997)

7.6.2 9 application repeat insult patch test – 1.6% notified chemical

TEST SUBSTANCE	Gel containing 1.6% of the notified chemical.
METHOD	The test was conducted according to HRL Standard Protocol No. 100 and the Informed Consent were approved by the New England Institutional Review Board (NEIRB)
Study Design	Human Repeated Insult Patch Test
Study Group	238 subjects (81 male, 157 female, age range 18 – 69); 210 completed the study.
Vehicle	Not provided
Induction Procedure	The induction phase consisted of 9 consecutive applications of the test substance under 24 hour occlusive conditions for approximately 3 weeks. At 48 hour intervals the patch sites were evaluated and an identical patch applied to the same site.
Rest Period	Approximately 2 weeks
Challenge Procedure	Identical patches were applied to sites previously unexposed to the test subject. The patches were removed after 24 hours and the sites graded. The sites were graded again at 48, 73 and 96 hours.
Remarks - Method	One subject did not have a 24 hour reading, three subjects did not have 48 hour reading, another three subjects did not have 72 hour reading and nine subjects did not have 96 hour reading. A verbal report from the subjects who missed the 96 hour reading indicated that there were no reaction present. No subject discontinued due to test material reaction.
RESULTS	
Remarks - Results	During the induction phase, two subjects exhibited erythema plus oedema reactions; their test sites were changed. The new test site exhibited no reaction. Other subjects exhibited low-level, transient reactions. At challenge phase, low-level, transient reactions were observed. The cause of the oedematous reaction in two subjects during induction phase was not further investigated.
CONCLUSION	The gel containing 1.6% of the notified chemical showed no evidence of sensitisation under the conditions of the test.
TEST FACILITY	Harrison Research Laboratories (2003b)

7.7 Irritation – eye

TEST SUBSTANCE	Capryloyl Glycine (Lipacide C8G Batch 98-1627) diluted to 5% with distilled water neutralised to pH 7 with sodium hydroxide.
METHOD	EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3M
Observation Period	The test animals were observed for 72 hours after the administration of the test substance if there is no evidence of irritation.
Remarks – Method	Observation times were 1 hour 24 hour 48 hour and 72 hour 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	0.7	0.3	0.3	1	4 day	0
Conjunctiva: chemosis	0	0	0	1	1 day	0
Conjunctiva: discharge	0	0	0	2	1day	0
Corneal opacity	0	0	0	0	0	0
Iridial inflammation	0	0	0	0	0	0

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

Remarks – Results: One hour after instillation of the substance Capryloyl Glycine (diluted 5% in distilled water) at the dose of 0.1 mL into the right eye of three rabbits, the outbreak of slight enanthemae with slight lacrimation occurred in all the animals and a slight swelling (in only one rabbit) 24 hours after instillation, only a slight redness of the conjunctiva was still observed in the three animals.

The reversibility was complete in less than 48 hours in two rabbits and in less than 72 hours in the third.

CONCLUSION: Caproyl Glycine as a 5% solution in distilled water is slightly irritating to the eye.

TEST FACILITY: EVIC-CEBA (1998)

7.8.1 Skin sensitisation

TEST SUBSTANCE: Capryloyl Glycine 100% (Lipacide CG powder Lot 89303001).

METHOD: OECD TG 406 Skin Sensitisation – Magnusson and Kligman method.

Species/Strain: Guinea pig/ Hartley

PRELIMINARY STUDY: Maximum Non-irritating Concentration:
intradermal:
topical: 100%, and 50% 25% and 12.5% in Vaseline oil

MAIN STUDY

Number of Animals: Test Group: 15 Control Group: 15

Induction phase: Induction Concentration:
intradermal injection
topical application Test 0.5g (Capryloyl glycine),
Control 0.5g (Vaseline oil)

Signs of Irritation: No sign of irritation noted in test animals

CHALLENGE PHASE

1st challenge: topical application: 0.5mL of MNIC (25% in Vaseline oil
topical application: 0.5mL of ½ MNIC (12.5%) in Vaseline oil

2nd challenge: topical application:

Remarks – Method: No significant protocol deviations

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	0.5mL of MNIC (25%)	0	0		
	0.5mL of ½ MNIC (12.5%)	0	0		
Control Group	0.5mL of MNIC (25%)	0	0		

0.5mL of ½ MNIC (12.5%)	0	0

Remarks – Results: No reactions were noticed in either the treated or control animals at any of the concentrations tested attributable to sensitisation was recorded during the examination following the removal of the occlusive dressing (challenge phase).

CONCLUSION: Capryloyl glycine (Lipacide CG Lot 89303001) did not induce any macroscopic reaction which could be related to sensitisation in the albino guinea pig. The material may be therefore regarded as Hypoallergenic.

TEST FACILITY: Biogir SA (1991).

7.8.2 Skin sensitisation

TEST SUBSTANCE: Capryloyl Glycine (Lipacide C8G Batch No 99088001) was tested as a powder

METHOD: Method according to Sato et al. A modified technique of guinea pig testing to identify delayed hypersensitivity allergens" Contact Dermatitis 1981: 7:225-237 (Munksgaard Copenhagen).

Species/Strain: Guinea pig/ Dunkin-Hartley ex David Hall Limited Burton on Trent UK.

PRELIMINARY STUDY: Maximum Non-irritating Concentration:
intradermal: not done as the product is a powder
topical: done in distilled water at 25%, 50% and 75%

MAIN STUDY

Number of Animals: Test Group: 10F Control Group: 10F

induction phase: Induction Concentration:
intradermal injection not performed
topical application: 25%, 50% and 75% of test product in distilled water applied as 0.1mL to four absorbent lint pads to abraded skin under impermeable surgical tape for each dilution for 24 hours

Signs of Irritation: No sign of irritation noted in test animals

CHALLENGE PHASE

1st challenge: topical application: 0.4mL of 25% and 10% in distilled water

2nd challenge: topical application:

Remarks – Method: No significant protocol deviations

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	25%	0 in 10	0		
	10%	0 in 10	0		
Control Group	25%	0 in 10	0		
	10%	0 in 10	0		

Remarks – Results: No skin reactions were noted at the test material challenge sites or vehicle control sites of the test and control group animals at the 24 and 48 hour observations.

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

TEST FACILITY: Safepharm Laboratories (1999b)

7.9 Genotoxicity – bacteria

TEST SUBSTANCE	Capryloyl Glycine (Lipacide C8G Batch 99056001)
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *Escherichia coli :* WP2uvrA
Metabolic Activation System	S9 Mix
Concentration Range in Main Test	a) With metabolic activation: 0-5000 µg/plate. b) Without metabolic activation: 0-5000 µg/plate.
Vehicle	Dimethyl sulphoxide
Remarks – Method	100 uL of the test article solution was administered. Evaluation criteria was if a greater than two fold increase in revertant count is observed in two experiments than this is taken as evidence of a positive response.
RESULTS	
	Under the experimental conditions employed no significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, with any dose of the test material up to the maximum dose of 5000 ug/plate, either with or without metabolic activation..
	No test material particulate precipitate was observed at any of the doses in the presence or absence of S9 mix.
	All the positive controls used in the test induced marked increases in the frequency of revertant colonies thus confirming the activity of the S9 mix and the sensitivity of the bacterial strains
CONCLUSION	The notified chemical was considered not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Safepharm Laboratories Limited (1999c)

8. ENVIRONMENT

8.1. Environmental fate

No test data for environmental fate endpoints were submitted. Modelled results are discussed in Section 9.1.1 below.

8.2. Ecotoxicological investigations

No ecotoxicity test data were submitted. Modelled and analogue data are discussed in Section 9.1.2 below.

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

Based on physico chemical properties provided in Section 6 the notified chemical is readily soluble and only slightly volatile.

The notifier did provide modelling results for biodegradation, and these results have been confirmed. The modelling software used is the US EPA EPIWIN software (US EPA, 2000). The models referred to in this and the next section are components of EPIWIN.

QSAR modelling (EPA BIOWIN v 4.0) predicts that the notified chemical is expected to exhibit a primary biodegradation time frame in the order of days. Both MITI linear and non-linear models predict that the chemical will be readily biodegradable.

The bioconcentration factor (BCF) has been modelled to be 2.26 (EC, 2003) and 3.16 (BCFWIN v2.14). Therefore, the notified chemical is not expected to bioconcentrate.

The Henry's Law Constant is predicted to be 2.92×10^{-10} based on the vapour pressure/water solubility ratio, so removal from water bodies through volatilisation is only expected to be very slight.

In LTD/1124 250 kg of notified chemical was to be imported per year. With the extension this rises to 750 kg per year, necessitating a recalculation of the PEC and PNEC values.

Release through sewer can potentially occur in all regions of Australia for this consumer chemical. Consequently, predicted environmental concentrations (PEC) have been derived for both coastal and inland areas with sewage treatment plant (STP) releases to either ocean or river (DEH, 2003). Worst case assumptions used in estimating these concentrations include:

- All imported product is ultimately released to sewer (ie, no absorption by skin; no exporting of product)
- Release occurs over 365 days of the year
- There is no removal in the STP through biodegradation, adsorption or volatilisation.

The following PECs are determined:

PECocean	0.05 μg/L
PECriver	0.5 μg/L

Assuming inherent biodegradability, SIMPLETREAT (EC, 2003) predicts that 41% of this chemical will be removed through biodegradation in the STP prior to release, so actual expected concentrations could be significantly less than those above.

9.1.2. Environment – effects assessment

While no measured data are available for the notified chemical, one test result of a suitably close analogue (N-Methyl-N-(1-oxododecyl)glycine, Sodium salt) obtained from the US EPA Aquire Database shows a 48 h LD50 of 28.97 mg/L for brine shrimp (*Artemia* sp.).

Results of ECOSAR modelling for neutral organic acids suggest the chemical is not toxic to aquatic species with the following results obtained:

ECOSAR Class	*Organism*	*Duration*	*End Pt*	*Predicted mg/L (ppm)*
Neutral Organic SAR (Baseline Toxicity)	Fish	14-day	LC50	1240.893
--> Acid moeity found: Predicted values multiplied by 10				
Neutral Organics-acid	Fish	96-hr	LC50	7729.912
Neutral Organics-acid	Daphnid	48-hr	LC50	7859.130
Neutral Organics-acid	Green Algae	96-hr	EC50	4702.995
Neutral Organics-acid	Fish	30-day	ChV	880.997
Neutral Organics-acid	Daphnid	16-day	EC50	289.051
Neutral Organics-acid	Green Algae	96-hr	ChV	303.120

Based on analogue data, it appears ECOSAR may underestimate toxicity. Given the uncertainty, a predicted no effect concentration (PNEC) for the aquatic compartment may be obtained using the analogue result and applying an assessment factor of 1000.

The resulting PNECaquatic is determined to be 28.97 μg/L.

No sediment or terrestrial PNEC has been calculated as there is not expected to be any significant exposure to these compartments.

9.1.3. Environment – risk characterisation

Aquatic: PEC/PNEC ratios for ocean and river exposure are determined to be and respectively. These are worst case, as they assumed no removal in the STP even though degradation would be expected to occur. The PEC/PNEC calculations are both well below 1 indicating the potential for adverse impacts on aquatic biota is small at the proposed import levels.

Sediment: The chemical is not expected to sorb strongly to sediment, so exposure to sediment organisms is unlikely to result in concentrations where adverse effects are found. Consequently, the risk to sediment organisms is expected to be small.

Terrestrial: Exposure to the soil through use is not expected. SIMPLETREAT predicts little to no binding to sludge in the STP, therefore, exposure through application of sewage sludge to agricultural land is not expected. Exposure to soil organisms is unlikely to result in concentrations where adverse effects are found. Consequently, the risk to these organisms is expected to be small.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Warehouse workers will handle the finished products containing the notified chemical while contained in their outer carton. Retail workers will handle the products in their retail packaging. These workers are unlikely to be exposed to the notified chemical except when plastic containers are damaged or punctured. Similarly, exposure to the notified chemical during transport of the product except in the event of transport accident.

The use of personal protective equipment (PPE) is not mandatory. However, PPE will be used and selected commensurate to work responsibilities.

Exposure of workers involved in the transport and storage of the neat notified chemical in the 20 kg import containers should only occur in the event of an accident. Following receipt of these containers, weighing out and addition to mixing vessels may result in exposure from accidental drips and spills. This exposure should be intermittent and the frequency of spillage should be low. Inhalation exposure should be precluded by the low volatility of the notified chemical and the use of local exhaust ventilation to capture dust. If spills are cleaned up in a way to avoid dust generation eg industrial vacuum cleaner or use of a dilute alkali solution as recommended I the MSDS, inhalation exposure should be low.

Once in the mixing vessels exposure of workers will be low because of the low concentration of notified chemical in the mixture and the low probability of breach of the system containment. Packing of finished products is predominantly automatic and exposure of packers is unlikely.

9.2.2. Public health – exposure assessment

The public exposure to the personal care products containing the notified chemical will be widespread and repeated. During use, 0.8 g/day of the facial gels containing the notified chemical is expected to be applied twice daily by dermal route. Assuming 20% of the product (containing 2% notified chemical) is absorbed by the skin, the consumer would be exposed to 6.4 mg/day notified chemical, which is equivalent to a systemic exposure of 0.107 mg/kg bw for a 60 kg female.

Other uses for products compounded from neat notified chemical are somewhat undefined but used as a leave-on hair conditioner would involve applying approximately 14 g of conditioner 2 days per week. Therefore, the notified chemical would be applied on average at 80 mg per day or 0.425 mg/kg bw/day for a 60 kg female assuming 20% absorption.

Overall, the public exposure to the notified chemical is low due to the low frequency of use, the low concentration (up to 2%) of the notified chemical present in the products, and the expected low systemic exposure.

9.2.3. Human health - effects assessment

The notified chemical has low oral toxicity in rats when dosed for 10 consecutive days. The study design did not allow for the determination of a No Observed Effect Level (NOEL); however, mortalities were observed at all doses. The toxicity is assumed to be of physical effects on the gastro intestinal tract due to large accumulation of test materials in animals, and no immediate toxicity was seen at high dose.

A number of studies to investigate the irritation potential of the notified chemical at concentrations between 1 to 10 have been carried out using leghorn eggs, red blood cell and human volunteers. The tests on eggs and red blood cells showed no evidence of irritation potential. In human volunteers, slight irritating effects were observed which were characterised by low level transient irritation effects, such as dryness and slight oedema. There was no evidence to show that the notified chemical at 1.6 and 5% is capable of eliciting sensitisation reaction based on the results obtained from two independent human volunteer studies.

Additional studies showed that the notified chemical was a slight eye irritant in rabbits at 5%, was not a skin sensitiser in guinea pigs and was not mutagenic in bacteria.

On the basis of the data supplied, there is insufficient information to classify the notified chemical as a hazardous substance according to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2002).

9.2.4. Occupational health and safety – risk characterisation

When the notified chemical is imported as a component of facial gels there is no manufacture, reformulation and packaging of the products containing it in Australia. Worker exposure to the notified chemical is expected to be low since warehouse, retail and transport workers will handle the finished products containing the notified chemical while contained in their outer packaging.

When the notified chemical is imported neat, significant exposure should only be possible during initial weighing and transfer operations as a result of spillage. Good general ventilation and local exhaust ventilation should preclude inhalation exposure during weighing, transfer and spillage. If spills are cleaned up via industrial vacuum cleaner and cleaning the affected area with dilute alkali as recommended in the MSDS, inhalation exposure should be low. Dermal exposure may result from infrequent spillage.

Due to the low hazard of the notified chemical and the low potential for exposure, the risk posed by the notified chemical to occupational health and safety is expected to be low.

9.2.5. Public health – risk characterisation

Members of the public will make dermal contact with the personal care products containing the notified chemical. Assuming 20% dermal absorption, systemic exposure would be 0.107 mg/kg bw for a 60 kg female using facial gels and a maximum of 0.425 mg/kg bw/day using leave-on hair conditioner, which is much lower compared with the subacute oral LD50 in rats (>10000 mg/kg bw), and would provide an adequate margin of safety. Although mortalities were observed at all doses in the subacute oral study, the toxicity is assumed to be due to physical effects related to large accumulation of test material in the gastro intestinal tract of treated animals.

Based on the expected low toxicological hazard, low exposure during use, and the low concentration of the notified chemical in facial gels, the risk to public health is considered low.

10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS

10.1. Hazard classification

Based on the available data there is insufficient information to classify the notified chemical as a hazardous substance according to the NOHSC *Approved Criteria for Classifying Hazardous Substances*.

As a comparison only, the classification of 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.

There are insufficient measured data to classify the notified chemical in accordance with GHS classification. However, based on the evidence available for environmental assessment, the notified chemical could tentatively be classified as Acute III with the corresponding Hazard Statement "Toxic to aquatic life." No chronic classification is necessary due to the predicted biodegradation and low logKow.

10.2. Environmental risk assessment

On the basis of the PEC/PNEC ratio:

The chemical is not considered to pose a risk to the environment based on its reported use pattern.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

There is Low Concern to occupational health and safety under the conditions of the occupational settings described.

10.3.2. Public health

There is No Significant Concern to public health when used as a component of facial gels.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the notified chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 2003). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

The labels for the notified chemical provided by the notifier were in accordance with the NOHSC *National Code of Practice for the Labelling of Workplace Substances* (NOHSC, 1994). The accuracy of the information on the labels remains the responsibility of the applicant.

12. RECOMMENDATIONS

CONTROL MEASURES

Occupational Health and Safety

- No specific engineering controls, work practices or personal protective equipment are required for the safe use of the notified chemical itself, however, these should be selected on the basis of all ingredients in the formulation.

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

- A copy of the 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.

Environment

Disposal

- Packaging containing residues of the end use product should be disposed of to landfill with household waste.

Emergency procedures

- Spills/release of the notified chemical should be swept up and placed in suitable receptacles for recovery or disposal.

12.1. Secondary notification

The Director of Chemicals Notification and Assessment 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, a full suite of toxicity and ecotoxicity data including a biodegradation study should be provided.

or

(2) Under Section 64(2) of the Act:

- if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

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