File No: LTD/1849

May 2016

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Glycine, *N*-methyl-*N*-(1-oxododecyl)-, 1-methylethyl ester (INCI name: Isopropyl Lauroyl Sarcosinate)

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment.

This Public Report is also available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

Street Address:	Level 7, 260 Elizabeth Street, SURRY HILLS NSW 2010, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX:	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

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SUMMARY

The following details will be published in the NICNAS *Chemical Gazette:*

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/1849	L'Oreal Australia Pty Ltd	Glycine, *N*-methyl-*N*-(1-oxododecyl)-, 1-methylethyl ester (INCI name: Isopropyl Lauroyl Sarcosinate)	ND*	≤ 1 tonne per annum	Cosmetic ingredient

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

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

Based on the available information, when used for the proposed uses and concentrations, the notified chemical is not considered to pose an unreasonable risk to public health.

Environmental risk assessment
On the basis of the reported use pattern and low import volume, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical during reformulation processes:
  - Avoid contact with eyes and skin

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical during reformulation processes:
  - Eye protection
  - Coveralls, impervious gloves

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

- A copy of the (M)SDS should be easily accessible to employees.

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)*

as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Public Health

- Product formulators should exercise due care when using the notified polymer in cosmetic products given its potential ability to enhance the dermal penetration of other chemicals in the formulation.

- Suppliers should ensure that amine levels in the notified chemical are minimised, in order to reduce the risk of nitrosamine formation.

Disposal

- Where reuse or recycling are not appropriate, dispose of the notified chemical in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

Emergency procedures

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

Regulatory Obligations

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

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
- the importation volume exceeds one tonne per annum notified chemical;
- the concentration of the notified chemical exceeds or is intended to exceed 10% in leave-on and rinse-off cosmetic products.
- information becomes available on the dermal absorption of the notified chemical.
- additional information becomes available on the genotoxicity of the notified chemical.

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from cosmetic ingredient, or is likely to change significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

(Material) Safety Data Sheet
The (M)SDS of the notified chemical and products containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
L'Oreal Australia Pty Ltd (ABN: 40 004 191 673)
564 St Kilda Road,
Melbourne VIC 3004

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: analytical data, degree of purity, impurities, use details, site of manufacture/reformulation, study references.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for all physico-chemical endpoints.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Canada (2012)

2. IDENTITY OF CHEMICAL

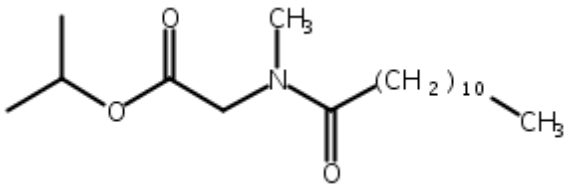
CAS NUMBER
230309-38-3

CHEMICAL NAME
Glycine, *N*-methyl-*N*-(1-oxododecyl)-, 1-methylethyl ester

OTHER NAME(S)
Isopropyl Lauroyl Sarcosinate (INCI name)

MOLECULAR FORMULA
C_{18} H_{35} N O_3

STRUCTURAL FORMULA



MOLECULAR WEIGHT
313.48 Da

ANALYTICAL DATA
Reference UV spectra was provided.

3. COMPOSITION

DEGREE OF PURITY
> 88%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: liquid to wax at ambient temperature

Property	Value	Data Source/Justification
Melting Point/Freezing Point	Not determined	The appearance of the chemical (as liquid or wax) suggests that the melting point is close to ambient temperature.
Boiling Point	> 386 °C at 101.3 kPa	Calculated
Density	920 kg/m^3 at 25 °C	(M)SDS
Vapour Pressure	2.27x10^{-7} kPa at 25 °C	Calculated
Water Solubility	2.627 × 10^{-4} g/L at 25 °C	Calculated using WSKOW v1.42 (US EPA, 2011)
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionalities; however, not expected to be significantly hydrolysed under environmental conditions (pH 4-9).
Partition Coefficient (n-octanol/water)	log Pow = 5.38	Calculated using KOWWIN v1.68 (US EPA, 2011)
Adsorption/Desorption	log K_{oc} = 3.788	Calculated using KOCWIN v2.00 (US EPA, 2011)
Dissociation Constant	Not determined	Contains no dissociable functionalities
Particle Size	Not determined	Liquid to wax at room temperature
Flash Point	198 °C	(M)SDS
Autoignition Temperature	Not determined	
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties

DISCUSSION OF PROPERTIES

Reactivity

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

Physical hazard classification

Based on the submitted physico-chemical data depicted in the above table, the notified chemical is not recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

5. INTRODUCTION AND USE INFORMATION

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

The notified chemical will not be manufactured within Australia. The notified chemical will be imported into Australia in neat form and as a component of finished cosmetic products at up to 10% concentration.

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

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

PORT OF ENTRY

Melbourne and Sydney

TRANSPORTATION AND PACKAGING

The notified chemical will be imported as a component of finished cosmetic products (at up to 10% concentration) in containers suitable for retail sale in ≤ 500 mL plastic/HDPE bottles or tubes. The finished cosmetic products are packaged in shipper cartons, which in turn are arranged in pallets inside sea containers. The notified chemical may also be imported in larger containers for blending in Australia.

USE
The notified chemical will be used as an ingredient of rinse-off and leave-on cosmetic products at up to 10% concentration, including those applied by spray.

OPERATION DESCRIPTION
The notified chemical will be imported in neat form and as a component of finished cosmetic products (up to 10%) into Australia.

Dockside and warehouse workers will transport the notified chemical and finished products containing the notified chemical from the wharf to the central distribution centres and place the pallets of products into the warehouse. Warehouse workers will be involved in transferring pallets in the central warehouse and operating a picking operation for stock to distributors at the retailer's central distribution depots.

In the case of the formulation process taking place in Australia, quantities of the products containing the notified chemical will be sampled and tested by a chemist for QA purposes. Production compounders will weigh an appropriate amount of the raw material into a separate container then add the amount directly into a flame proof mixing tank. Mixing and dispensing will be carried out in a closed system with flame proof mixers and pumps designed not to create aerosols or a dust hazard and earthed for static discharges.

Products containing the notified chemical (up to 10%) may be used by the public and in professions where the services involve the application of cosmetic products to clients (e.g. workers in beauty or hair salons).

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and Storage	4	12
Professional compounder	8	12
Chemist	3	12
Packers (Dispensing & Capping)	8	12
Store Persons	4	12
Salon workers	8	365

EXPOSURE DETAILS
Transport and storage
Dockside and warehouse workers are not expected to have any contact with the notified chemical, which is contained in sealed packages, except in the case of spills.

Reformulation
During formulation process, workers involved in weighing, mixing and dispensing (compounders) may experience dermal, ocular and inhalation exposure from drips, spills, splashes and weighing the material and adding to mixing tanks. Chemists may come into an accidental skin or eye contact with the notified chemical during sampling and testing for QA purposes. Workers are expected to use safety glasses with shields, gloves, and apron or coverall during formulation process. Adequate ventilation and appropriately located exhaust hoods will be also used in the workplace.

End-use
Exposure to the notified chemical in end-use products (at up to 10% concentration) may occur in professions where the services provided involve the application of cosmetic and personal care products to clients (e.g. hair dressers, workers in beauty salons). The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible. Such professionals may use some PPE to minimise repeated exposure, but this is not expected to occur in all workplaces. However, 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 to the notified chemical at up to 10% concentration is expected to be widespread and frequent through daily use of various cosmetic products. Exposure to the notified chemical will vary depending on individual use patterns. The main route of exposure will be dermal, as well as incidental ocular and inhalation exposures. Ingestion exposure (from the use of face and lip products) may also occur.

Exposure can be estimated using data on typical use patterns of cosmetic product categories in which the notified chemical may be used (SCCS, 2012; Cadby et al., 2002; ACI, 2010; Loretz et al., 2006). For the purposes of the exposure assessment, Australian use patterns for the various product categories are assumed to be similar to those in Europe. A lifetime average female body weight (bw) of 64 kg (enHealth, 2012) was used for calculation purposes.

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products that contain the notified chemical. This would result in a combined internal dose of 2.87 mg/kg bw/day. Specific use details of the notified chemical are considered exempt information.

6.2. Human Health Effects Assessment

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

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – Maximisation Test.	no evidence of sensitisation
Rat, repeat dose (gavage) toxicity – 28 days.	NOAEL of 200 mg/kg bw/day
Rat, effects on embryo-foetal development by oral route (gavage) (preliminary and main study)	NOAEL of 1000 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* chromosome aberration test – in chinese hamster V79 cells.	genotoxic
Genotoxicity – *in vivo* Mammalian erythrocyte micronucleus test	non genotoxic

Toxicokinetics, metabolism and distribution.

No toxicokinetic data is available for the notified chemical. The notified chemical has a molecular weight of 313 Da and a calculated partition coefficient (log Pow) of > 5, and therefore has potential to be absorbed via the dermal route (ECHA, 2012). The default absorption of 100% would be reduced to 10% if molecular weight was > 500 Da, using the same log Pow. Based on its structure, the notified chemical has a potential for surface activity and may enhance the penetration of other chemicals. The potential for penetration enhancement was identified for the similar chemical group, sarcosines and sarcosinates (CIR, 2001)

A review of alcohol ethoxylate surfactants, which have similarities to the notified chemical in being non-ionic, determined that skin penetration was low in a dermal penetration study on two human volunteers (HERA, 2009). Using radiolabelling, 2% or less absorption of ethoxylated lauryl alcohol was seen. A sarcosine surfactant, with some structural similarities to the notified chemical, showed < 1% absorption in an isolated skin model (Aioi et al, 1993), and up to 6% of lauramidopropyl betaine was absorbed through rat skin after 48 h (HERA, 2005). Prediction of dermal absorption of the notified chemical according to a model provided by the notifier (Gregoire et al 2009) was 1 to 5%. While there is uncertainty about the dermal absorption potential of the notified chemical, a value of 10% dermal absorption was assumed for quantitative risk assessment purposes.

Acute toxicity.

The notified chemical is of low acute toxicity by oral and dermal routes. No information on acute inhalation toxicity was provided.

Irritation and sensitisation.

Based on studies in rabbits, the notified chemical is a slight skin and eye irritant.

In a guinea pig maximisation test, the notified chemical showed no evidence of skin sensitisation.

Repeated dose toxicity.
A NOAEL of 200 mg/kg bw/day in male and female rats was determined from a 28 day repeated dose toxicity test in rats, based on increases in the liver weights of male and female rats treated at 1000 mg/kg bw/day and increases in kidney weights of female rats treated with 1000 mg/kg bw/day.

Reproductive/developmental toxicity
In an oral Prenatal Developmental Toxicity test carried out to OECD TG 414 in rats, a NOAEL of 1000 mg/kg bw/day was established for both maternal toxicity and embryo-foetal toxicity. Similar results were obtained in a preliminary test using fewer animals.

Mutagenicity/Genotoxicity.
The notified chemical was negative in an *in vitro* bacterial reverse mutation study.

An *in vitro* chromosome aberration test in Chinese Hamster V79 cells showed clear positive results in the presence of a metabolic activation system, but negative results without metabolic activation. An *in vivo* test for the same endpoint (mouse micronucleus assay in bone marrow) was negative. Although the access of the test substance to the bone marrow could not be demonstrated, adverse clinical signs in the test animals suggest that there was systemic exposure to the test substance.

On the basis of the available information, while the notified chemical is not expected to be clastogenic, this cannot be ruled out, given the positive result in the chromosome aberration study.

Formation of nitrosamines
A starting material (sarcosine) in the manufacture of sarcosines and sarcosinates, can be nitrosated to form a known animal carcinogen (CIR, 2001). However the nitrogen in the notified chemical is part of an amide group, which has low reactivity towards common nitrosating agents (SCCS, 2012). The notifier has advised that the level of amines (including sarcosine) present in the notified chemical is very low. Therefore the possibility of nitrosamine formation in the notified chemical is considered to be low.

Health hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Transport and storage
Workers may experience dermal and accidental ocular exposure to the notified chemical (at >88% concentration) during transport or storage.

Reformulation
Workers may experience dermal, ocular and inhalation exposure to the neat notified chemical during formulation processes. This exposure may occur during handling of the chemical, cleaning and/or maintenance of the equipment. Exposure may also extend to compounders and laboratory staff involved in the formulation of the end products containing the notified chemical and the sampling and quality control testing of these products.

The use of enclosed process and PPE (safety glasses with shields, gloves, apron or coverall), and adequate ventilation and appropriately located exhaust hoods if significant inhalation exposure is expected) is expected to be used during formulation processes.

Based on the use of measures used to mitigate exposure and the overall low toxicity of the notified chemical, the risk to workers from transport/storage and use of the notified chemical is not considered to be unreasonable.

End-use
Workers involved in professions where the services provided involve the application of cosmetic products containing the notified chemical to clients (e.g., hairdressers and beauty salon workers) may be exposed to the

notified chemical. The risk to these workers is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified chemical.

Such professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. For hairdressing salons, good ventilation would reduce exposure if hair spray is routinely used in a confined space. If PPE is used, the exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using the various cosmetic products containing the notified chemical. Based on the information available, the risk to workers associated with use of the notified chemical is not considered to be unreasonable.

6.3.2. Public Health

Members of the public will experience widespread and frequent exposure to the notified chemical through daily use of cosmetic products of leave on and rinse off products at up to 10% concentrations.

The potential systemic exposure to the public from the use of the notified chemical in cosmetic products was estimated to be 2.87 mg/kg bw/day. Using a NOAEL of 200 mg/kg bw/day, which was derived from an oral repeated dose toxicity study on the notified chemical, the margin of exposure (MOE) was estimated to be 70. A MOE value greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences. However, there is a considerable difference between the dose at which effects were seen (1000 mg/kg bw/day) and the next highest dose tested (200 mg/kg bw/day). Moreover, the increases in organ weights on which the NOAEL was based were not accompanied by histopathological changes or changes in clinical chemistry. The NOAEL is therefore expected to be < 1000 mg/kg bw/day. Overall the NOAEL of 200 mg/kg may represent a conservative NOAEL, therefore, the MOE of 70 is considered to be acceptable.

As the notified chemical may have the potential to enhance dermal absorption of other chemicals, care should be taken in formulating end-use products containing it. Minimising levels of amine impurities in the notified chemical would reduce the likelihood of hazardous nitrosamine formation. Further data on dermal absorption and toxicological information on genotoxicity and inhalation toxicity would reduce the uncertainty in these areas.

Based on the available information, the risk to the public associated with the use of the notified chemical at up to 10% in leave-on and rinse-off cosmetic products is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will not be manufactured in Australia. The notified chemical will be imported as a raw material for reformulation into cosmetic products, or as a component of finished cosmetic formulations in end-use packaging. Therefore, there is unlikely to be any significant release to the environment from transport and storage, except in the case of accidental spills or leaks. In the event of spills, the product containing the notified chemical is expected to be collected by inert absorbent material, and disposed of to landfill in accordance with local government regulations.

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

RELEASE OF CHEMICAL FROM USE

The notified chemical is a component of rinse-off and leave-on cosmetic formulations. The formulated products will be applied to the body, and will either be removed with tissues and disposed of to domestic garbage, or washed off the body with ultimate release to the sewer.

RELEASE OF CHEMICAL FROM DISPOSAL

It is estimated that a maximum of 1%, or up to 10 kg of the notified chemical, may remain in import containers, and a maximum of 3%, or up to 30 kg, in end-use containers once the consumer products are used up. Wastes and residue of the notified chemical in empty containers are likely either to share the fate of the container and be disposed of to landfill, or be released to sewer when containers are rinsed before recycling through an approved waste management facility.

7.1.2. Environmental Fate

Following its use in cosmetic formulations, the majority of the notified chemical is expected to enter the sewer system, before potential release to surface waters nationwide. Although the notified chemical has low calculated water solubility, it is readily biodegradable (88% in 28 days). For details of the environmental fate study, please refer to Appendix C.

Based on its low calculated water solubility and calculated adsorption coefficient (log K_{OC} = 3.788), the notified chemical is expected to partition to sludge and sediment at environmental pH. The notified chemical has the potential to bioaccumulate based on its low molecular weight, low water solubility and high calculated n-octanol/water partition coefficient (log P_{OW} = 5.38). However, bioaccumulation is unlikely based on its low bioconcentration factor (BCF = 45.87), calculated using BCFBAF v3.01 (US EPA, 2011), and its ready biodegradability. Therefore, in surface waters the notified chemical is expected to disperse and degrade through biotic and abiotic processes to form water and oxides of carbon and nitrogen.

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

7.1.3. Predicted Environmental Concentration (PEC)

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

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	0%	
Daily effluent production:	4,523	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.606	µg/L
PEC - Ocean:	0.061	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1,000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1,500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.606 µg/L may potentially result in a soil concentration of approximately 4.039 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of the notified chemical in the applied soil in 5 and 10 years may be approximately 20.19 µg/kg and 40.39 µg/kg, respectively.

7.2. Environmental Effects Assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h LL50 > 0.00125 mg/L (WAF*)	Not harmful to fish up to limit of water solubility
Daphnia Toxicity	487 h EL50 > 0.025 mg/L (WAF*)	Not harmful to *Daphnia* up to limit of water solubility

* Water Accommodated Fraction

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

7.2.1. Predicted No-Effect Concentration

The predicted no-effects concentration (PNEC) for the aquatic compartment has not been calculated since the notified chemical is not considered to be harmful to aquatic organisms up to the limit of its solubility in water.

7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) has not been calculated as a PNEC is not available. The notified chemical is readily biodegradable and is not expected to be bioaccumulative. On the basis of the maximum annual importation volume and assessed use pattern in cosmetic formulations, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified Chemical

METHOD: OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.

Species/Strain	Rat/Male and Female HanBr:WIST
Vehicle	PEG 300
Remarks - Method	GLP Compliance. No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3M	2000	0
2	3F	2000	0

LD50	> 2000 mg/kg bw
Signs of Toxicity	No clinical signs or toxicity were noted in all animals during the course of the study.
Effects in Organs	No macroscopic findings were observed at necropsy.
Remarks - Results	All animals survived until the scheduled termination Body weight gain of the animals was as expected.

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

TEST FACILITY: Exempt Information (2001d)

B.2. Acute toxicity – dermal

TEST SUBSTANCE: Notified Chemical

METHOD: OECD TG 402 Acute Dermal Toxicity.

Species/Strain	Rat/Han Brl:WIST
Vehicle	None
Type of dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5M, 5F	1840	0
2	5M, 5F	2000	0

LD50	>2000 mg/kg bw
Signs of Toxicity - Local	Slight scales on the back were observed in one female at 1840 mg/kg on test day 8 until test day 12. All other animals were without clinical signs.
Signs of Toxicity - Systemic	Two female animals lost weight slightly in the first 7 days after treatment but regained it in the next 7 days.
Effects in Organs	No macroscopic findings were observed at necropsy.
Remarks - Results	No deaths occurred during the study.

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

TEST FACILITY: Exempt Information (2002e)

B.3. Irritation – skin

TEST SUBSTANCE Notified Chemical

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion.

Species/Strain	Rabbit/New Zealand White
Number of Animals	1M, 2F
Vehicle	None
Observation Period	10 days
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0.67	1.67	0.67	2	< 7 d	0
Oedema	0.00	0.33	0.00	1	< 48 h	0

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

Remarks - Results No clinical signs of systemic toxicity were observed in the animals during the study and no mortality occurred.

Scaling was noted in two animals at 48 h, one animal at 72 h and one animal at 7 days.

CONCLUSION The notified chemical is slightly irritating to the skin.

TEST FACILITY Exempt Information (2002f)

B.4. Irritation – eye

TEST SUBSTANCE Notified Chemical

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.

Species/Strain	Rabbit/New Zealand White
Number of Animals	1M, 2F
Observation Period	1, 24, 48 and 72 h
Remarks - Method	No significant protocol deviations. One animal was treated prior to the other two.

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	0.67	0.33	0	1	≤ 48 h	0
Conjunctiva: chemosis	0	0	0	1	1 h	0
Conjunctiva: discharge	0	0	0	1	1 h	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	No clinical signs of systemic toxicity were observed in the animals during the study and no mortality occurred. No abnormal findings were observed in the cornea or iris of any animal at any reading. No staining of the treated eyes by the test substance was observed. A slight watery discharge was apparent in all animals at the 1-hour reading. Reddening of the sclera was seen in two animals at the 1 h observation only. The effects on the conjunctivae were no longer evident 72 hours after treatment, the end of the observation period tor all animals.
CONCLUSION	The notified chemical is slightly irritating to the eye.
TEST FACILITY	Exempt Information (2002g)

B.5. Skin sensitisation

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 406 Skin Sensitisation – Maximisation Test. EC Directive 96/54/EC B.6 Skin Sensitisation – Maximisation test.
Species/Strain	Guinea pig/Albino
PRELIMINARY STUDY	Maximum Non-irritating Concentration: 0.5% of the notified chemical (determined as a result of three pre-tests) intradermal: 1) 0.1 mL of 50% of the test substance in FCA (Freund's Complete Adjuvant/physiological saline). 2) 0.1 mL of 100%, 75%, and 50% in PEG 300 after one week of the first intradermal injection
MAIN STUDY	
Number of Animals	Test Group: 10M Control Group: 5M
Vehicle	PEG 300
Positive control	Not conducted in parallel with the test substance.
INDUCTION PHASE	Induction Concentration: 100% intradermal: 0.1 mL of 50% of the test substance in FCA (Freund's Complete Adjuvant/physiological saline). topical: 0.1 mL of undiluted test substance after the intradermal induction for 48 h (occlusive).
Signs of Irritation	Discrete or patchy erythema
CHALLENGE PHASE	
challenge	topical: 0.5% in PEG 300 (occlusive)
Remarks - Method	Two weeks after the epidermal induction, the control and test animals were challenged by epidermal application of 0.5% notified chemical in PEG 300 under occlusive dressings and evaluated after 24 and 48 hours after removing the dressings.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: 1st challenge*	
		24 h	*48 h*
Test Group	0.5%	0/10	0/10
Control Group	0.5%	0/5	0/5

Remarks - Results	No toxic symptoms were evident and no deaths occurred in the control or test animals. None of the test or control animals showed skin reactions after the challenge treatment at 0.5%.

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

TEST FACILITY Exempt Information (2002h)

B.6. Repeat dose toxicity

TEST SUBSTANCE Notified chemical

METHOD OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral).

Species/Strain	Rats/Wistar
Route of Administration	Oral
Exposure Information	Total exposure days: 28 days Dose regimen: Gavage concentrations of 0, 50, 200 and 1000 mg/kg bw/day for 7/7 days per week. 4 groups of 5M, 5F each
Vehicle	PEG 300
Remarks - Method	

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5M, 5F	0	0
low dose	5M, 5F	50	0
mid dose	5M, 5F	200	0
high dose	5M, 5F	1000	0

Mortality and Time to Death
No unscheduled mortality was observed in any treatment group.

Clinical Observations
There were no clinical signs of toxicity noted. There were no changes in the behavioural parameters functional performance including grip strength and locomotor activity that were considered treatment related.

No effects on food consumption were observed in any group during the period of the treatment.

No test item-related changes in body weight were observed during the test period.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
There were no changes considered to be toxicologically significant in any of the haematological, blood chemistry measured compared to the controls.

Effects in Organs
No macroscopic or microscopic abnormalities were detected for any treated rats.

At the dose of 1000 mg/kg bw/day, kidney weights were increased in females and liver weights were increased in both sexes.

Remarks – Results

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 200 mg/kg bw/day, based on the increases in the liver weights of male and female rats treated at 1000 mg/kg bw/day and increases in kidney weights of female rats treated with 1000 mg/kg bw/day.

TEST FACILITY Exempt Information (2002i)

B.7. Preliminary Study -Prenatal Development toxicity

TEST SUBSTANCE	Notified chemical
METHOD	Not stated – similar to OECD TG 414, using fewer animals
Species/Strain	Rats/Sprague-Dawley
Route of Administration	Oral – gavage
Exposure Information	Exposure: daily doses of 100, 300 or 1000 mg/kg /day from day 6 to day 19 post-coitum. Post-exposure observation period:
Vehicle	Corn oil
Remarks - Method	GLP Three groups of seven mated female rats received the test substance daily by gavage, from day 6 to day 19 post-coitum. One group of seven mated female rats received the vehicle alone (control group). On day 20 post-coitum, all the females were killed. The gravid uterus was weighed to allow calculation of the net body weight gain. All the foetuses were removed by hysterectomy, weighed, sexed and submitted to an external examination to check for malformations and/or variations. The dams were examined macroscopically.

RESULTS

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	7	0	0
2	7	100	0
3	7	300	0
4	7	1000	0

Mortality and Time to Death

No unscheduled mortality was observed in any treatment group.

Effects on Dams

No treatment-related effects were observed on the pre- or post-implantation loss, the foetal weight or the sex ratio at any dose-level.

Effects on Foetus

There were no external malformations or variations that were related to the treatment with the test substance. The number of live foetuses per female was similar in the control and treated groups. The sex ratio was similar in all the control and treated groups and close to the expected value of 50%.

Remarks – Results

The food consumption was similar in the control and the treated groups over the treatment period.

There were no treatment-related changes in body weight or body weight gain at any dose-level. The net body weight change was similar in the control and the treated groups.

The macroscopic findings observed among those commonly recorded in rats of this strain and age were: paleness of the liver and accentuated lobular pattern in one female of the high dose-group or dilatation of uterine horn in one non pregnant female of the low dose-group and were considered of spontaneous occurrence.

There was no abortion or total resorption in any group. There were no treatment-related clinical signs except for ptyalism (excessive production of saliva) in all the treated groups. This sign was not considered by the study author to represent an adverse effect.

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) was established as 1000 mg/kg bw/day in this study, based on no signs of embryo toxicity, foetotoxicity or teratogenicity at any dose-level.

TEST FACILITY Exempt Information (2002)

B.8. Prenatal Developmental toxicity

TEST SUBSTANCE Notified chemical

METHOD OECD TG 414 Prenatal Development Toxicity Study
Species/Strain Rats/Sprague-Dawley
Route of Administration Oral – gavage
Exposure Information Exposure: daily doses of 100, 300 or 1000 mg/kg /day from day 6 to day 19 post-coitum.
Post-exposure observation period:
Vehicle Corn oil
Remarks - Method Three groups of 24 mated female rats received daily the test substance, by gavage from day 6 to day 19 post-coitum.
One group of 24 mated female rats received the vehicle alone (control group).
On day 20 post-coitum, all the females were killed. The gravid uterus was weighed to allow calculation of the net body weight gain.
All the foetuses were removed by hysterectomy, weighed, sexed and submitted to an external examination to check for malformations and/or variations. The dams were examined macroscopically.

RESULTS

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	24	0	0
2	24	100	0
3	24	300	0
4	24	1000	0

Mortality and Time to Death
No unscheduled mortality was observed in any treatment group.

Effects on Dams
The food consumption was similar in the control and the treated groups over the treatment period. There were no treatment-related changes in body weight or body weight gain at any dose-level. Ptyalism noted in all treatment groups was attributed to the gavage method of administration.

No treatment-related effects were observed on the pre- or post-implantation loss, the foetal weight or the sex ratio at any dose-level. There was no abortion or total resorption in any group. Post-implantation loss was higher in the 1000 mg/kg bw/day group than the controls. However the change was not considered to be treatment-related as it was not clearly dose related, not statistically significant, and the high dose value was within historical controls

Effects on Foetus
There was no external, tissue or skeletal malformations or variations that were related to the treatment with the test substance. The number of live foetuses per female was similar in the control and treated groups. The foetal body weight was similar in all groups.

Remarks - Results
No treatment-related microscopic post-mortem findings were observed at any dose level.

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) for maternal toxicity and for embryofetal toxicity was established as 1000 mg/kg bw/day in this study.

TEST FACILITY Exempt Information (2003)

B.9. Genotoxicity – bacteria

TEST SUBSTANCE Notified Chemical

METHOD
OECD TG 471 Bacterial Reverse Mutation Test.
EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Pre incubation procedure

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, and *E. coli*: WP2uvrA.
Metabolic Activation System	S9 fraction from phenobarbitone/β-naphthoflavone induced rat liver.
Concentration Range in Main Test	a) With metabolic activation: 3 - 5,000 µg/plate b) Without metabolic activation: 3 - 5,000 µg/plate
Vehicle	Dimethyl sulphoxide
Remarks - Method	No significant protocol deviations. GLP Compliance.

A preliminary test was conducted using all strains tested at different concentrations (33, 100, 333, 1,000, 2,500 and 5,000 µg/plate) for toxicity and mutation induction. The main test was conducted at concentrations (156.25, 312.5, 625, 1,250, 2,500 and 5,000 µg/plate).

The pre-experiment is reported as main experiment (for each strain and dose level including the controls, three plates were used).

Vehicle and positive controls were used in parallel with the test material.
Positive controls: i) without S9: sodium azide, NaN_3 (used as the positive control for the tester strains: TA100, TA1535), 4-nitro-o-phenylene-diamine, 4-NOPD (TA1537, TA98) and methyl methane sulfonate, MMS (WP2uvrA); ii) with S9: 2-aminoanthracene, 2-AA (TA1535, TA1537, TA98, TA100, and E. coli: WP2uvrA).

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 2,500 (TA1535, TA1537)		Not specified	negative
Test 2		≥ 2,500 (TA1537)	Not specified	negative
Present				
Test 1	≥ 2,500 (TA1535, TA1537)		Not specified	negative
Test 2		≥ 2,500 (TA1537, TA100)	Not specified	negative

Remarks - Results
The plates incubated with the test substance showed normal background growth up to 5000 µg/plate with and without S9 mix in both experiments.

A small reduction in the number of revertants at 2,500 and 5,000 µg/plate concentrations in the pre-experiment indicating minor toxic effect were observed in strains TA1535 and TA1537 with and without S9 mix. In the

main test, minor toxic effects were observed in strain 1537 with and without S9 Mix and in TA100 only with S9 mix.

No significant increases in the frequency of revertant colonies were recorded for any of the strains of bacteria, at any dose level either with or without metabolic activation. The positive controls performed as expected, confirming the validity of the test system.

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

TEST FACILITY Exempt Information (2002j)

B.10. Genotoxicity – in vitro

TEST SUBSTANCE Notified Chemical

METHOD OECD TG 473 In vitro Mammalian Chromosome Aberration Test.

Species/Strain	Chinese Hamster
Cell Type/Cell Line	V79/T5
Metabolic Activation System	Phenobarbitone/β-naphthoflavone induced rat liver (S9 homogenate)
Vehicle	Dimethyl sulphoxide
Remarks - Method	No significant protocol deviations. GLP Compliance. Vehicle and positive controls were used in parallel with the test material. Positive controls: i) without S9: Ethylmethane sulfonate (EMS); ii) with S9: Cyclophosphamide (CPA).

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0.8, 1.6, 3.1, 6.3*, 12.5*, 25.0*, 37.5, 50.0 and 75.0	4h	18h
Test 2 (18h)	0.8, 1.6, 3.1*, 6.3*, 12.5*, 25.0	18h	18h
Test 2 (28h)	3.1, 6.3, 12.5*, 25.0	28h	28h
Present			
Test 1	12.5, 25.0*, 50.0*, 75.0, 100.0* and 150.0	4h	18h
Test 2	12.5, 25.0*, 50.0*, 75.0*, 100.0 and 150.0	4h	28h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (μg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 12.5		Not specified	negative
Test 2 (18h)		≥ 6.3	Not specified	negative
Test 2 (28h)		≥ 12.5	Not specified	negative
Present				
Test 1	≥ 100.0		Not specified	positive
Test 2		≥ 25.0	Not specified	positive

Remarks - Results No statistically significant increases in polyploidy cells were observed.

In both experiments, toxic effects indicated by reduced cell numbers and /or mitotic indices were observed.

In the presence of S9 mix, statistically significant and biologically relevant increases in the number of cells carrying structural chromosomal aberrations were observed after treatment with the test substance in the presence of S9 mix. This occurred at the highest dose tested, for both the 18h and 28 h preparation intervals. The increases in aberrant cells were accompanied by an increase in the number of cells containing exchanges.

The positive and vehicle controls gave satisfactory responses confirming the validity of the test system.

CONCLUSION The notified chemical was clastogenic to V79 cells treated in vitro under the conditions of the test.

TEST FACILITY Exempt Information (2002k)

B.11. Genotoxicity – in vivo

TEST SUBSTANCE Notified Chemical

METHOD OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
Species/Strain Mouse/NMRI
Route of Administration Oral
Vehicle Corn oil
Remarks - Method GLP Compliance.

A preliminary toxicity study was conducted, in which mice were treated with the test substance at 2,000 mg/kg bw. The animals (2m, 2F) were examined for acute toxic symptoms at intervals of approximately 1, 2-4, 6, 24, 30 and 48h.

In the main study, animals were treated with the test substance (at 0, 500, 1,000, and 2,000 mg/kg) and samples of bone marrow were taken at 24 hours (and at 48 hours for the high dose group).

A positive control (cyclophosphamide) study was conducted in parallel with the test substance.

The incidence of micronucleated polychromatic erythrocytes per 2,000 polychromatic erythrocytes was determined.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	5M, 5F	0	24h
II (low dose)	5M, 5F	500	24h
III (mid dose)	5M, 5F	1000	24h
IV (high dose)	12M, 12F	2000	24h & 48h
V (positive control, CP)	5M, 5F	40	24h

CP=cyclophosphamide.

RESULTS
Doses Producing Toxicity (≥ 2000 mg/kg bw). No significant increase in the number of normochromatic erythrocytes (NCEs) compared to the vehicle control was observed, indicating that the test substance did not induce any cytotoxic effects on the bone marrow. However, some animals of the high dose level group showed adverse clinical signs after treatment, including reduction of spontaneous activity, eyelid closure and ruffled fur, indicating systemic exposure to the test substance.
Genotoxic Effects No significant increases in the frequency of micronucleated polychromatic erythrocytes were recorded for both sexes at any dose level 24 hours after dose administration and in males at 48 hours after dose administration

	(compared to control groups). The controls produced satisfactory responses, thus confirming the validity of the test system. (The positive control showed a substantial increase of induced micronucleus frequency).
CONCLUSION	The notified chemical was not clastogenic under the conditions of this in vivo micronucleus test.
TEST FACILITY	Exempt Information (2002l)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Theoretical Oxygen Demand (ThOD)
Remarks - Method	No significant deviation in protocol. Ultrasound dispersion was used to treat the test substance for 15 minutes prior to use to obtain a homogeneous suspension.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
0	0	0	0
7	48-58	7	78
14	65-81	14	85
21	75-94	21	88
28	79-99	28	88

Remarks - Results	All validity criteria for the test were satisfied. The percentage degradation of the reference compound, sodium benzoate, surpassed the threshold level of 60% by 7 days (78%) and reached 88% degradation by 28 days. Therefore, the test indicates the suitability of the inoculums. The test substance attained ≥ 79% degradation by 28 days, and attained ≥ 60% degradation by 12 days (i.e. within the 10-day window). Therefore, the test substance is classified as readily biodegradable according to the OECD (301 F) guideline.
CONCLUSION	The test substance is readily biodegradable.
TEST FACILITY	Exempt Information (2002c)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test – Static.
Species	*Brachydanio rerio* (zebra fish)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks – Method	No significant deviation in protocol. Due to the low aqueous solubility of the test substance, the test substance was prepared as a Water Accommodated Fraction (WAF), using an undiluted filtrate of a supersaturated dispersion of the test substance (100 mg/L loading rate).

RESULTS

Concentration mg/L	*Number of Fish*	*Mortality (%)*

Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	Control	7	0	0	0	0	0
100	0.00125	7	0	0	0	0	0

LL50	> 0.00125 mg/L (WAF) at 96 hours.
NOEL	0.00125 mg/L (WAF) at 96 hours.
Remarks – Results	All validity criteria for the test were satisfied. The test solutions were not renewed during the 96 h test period. The actual concentrations of the test substance were measured at 0, 48 and 96 hours during the 96 h test period. The test substance was measured to be 0.00125 mg/L at 0 h, and below the limit of quantification (LOQ; < 0.001 mg/L) for all other samples. No abnormalities in behaviour or appearance were observed. The 96 h LC50 and NOEC for fish were determined to be > 0.00125 mg/L (WAF) and 0.00125 mg/L (WAF), respectively, based on measured concentrations.
CONCLUSION	Under the study conditions, the notified chemical is not considered to be harmful to fish up to the limit of its water solubility.
TEST FACILITY	Exempt Information (2002a)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – Static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	No significant deviation in protocol. Due to the low aqueous solubility of the test substance, the test substance was prepared as a Water Accommodated Fraction (WAF), using an undiluted filtrate of a supersaturated dispersion of the test substance (100 mg/L loading rate).

RESULTS

Concentration mg/L		*Number of D. magna*	*Cumulative Immobilised (%)*	
Nominal	*Actual*		*24 h*	*48 h*
Control	Control	20	0	0
100	0.025	20	0	0

EL50	> 0.025 mg/L (WAF) at 48 hours
NOEL	0.025 mg/L (WAF) at 48 hours
Remarks - Results	All validity criteria for the test were satisfied. The test solutions were not renewed during the 48 h test period. The actual concentrations of the test substance were measured at 0 and 48 hours during the 48 h test period. The test substance was measure to be 0.0286 mg/L 0.0213 mg/L at 0 and 48 h, respectively (mean 0.025 mg/L). No abnormalities in behaviour or appearance were observed. The 48 h EC50 and NOEC for daphnids were determined to be > 0.025 mg/L (WAF) and 0.025 mg/L (WAF), respectively, based on measured concentrations.
CONCLUSION	Under the conditions of the study, the notified chemical is not considered to be harmful to daphnids up to the limit of its water solubility.
TEST FACILITY	Exempt Information (2002b)

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