File No: LTD/1481

January 2011

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

LILYFLORE

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

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

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

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Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Firmenich Limited (ABN 86 002 964 794)
73 Kenneth Road,
Balgowlah NSW 2093

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: Chemical name, Other names, CAS number, Molecular and structural formulae, Molecular weight, Identity and weight percent of non-hazardous impurities, Spectral data and Degree of purity.

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)
LVCR/86

NOTIFICATION IN OTHER COUNTRIES
Switzerland, USA, EU, Philippines, Canada, Korea and China.

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
LILYFLORE (notified chemical)

3. COMPOSITION

DEGREE OF PURITY 92-99%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: White liquid (may form chrystals)

Property	Value	Data Source/Justification
Melting Point	44.3°C	Measured
Boiling Point	279°C at 97.3 kPa	Measured
Density	1070 kg/m^3 at 20°C	Measured
Vapour Pressure	9.8x10^{-5} kPa at 25°C	Measured
Water Solubility	0.609 g/L at 20°C, pH 9	Measured
Hydrolysis as a Function of pH	$t_{½}$ >1 year at 25°C, pH 4-9	Measured
Partition Coefficient (n-octanol/water)	log K_{OW} = 2.94 at 21°C	Measured
Adsorption/Desorption	log K_{OC} = 2.7 at 25°C	Measured
Dissociation Constant	Not determined	The notified chemical does not contain functionality that is expected to dissociate under environmental conditions
Particle Size	N/A	The notified chemical is a liquid.
Flash Point	142°C at 101.3 kPa	Measured
Flammability	Not highly flammable	Measured
Autoignition Temperature	>400°C	Measured
Explosive Properties	Not likely to be explosive	The chemical structure of the notified chemical does not contain functional groups that would have explosive properties.
Surface Tension	46.5 mN/m at 20°C	Measured
Oxidizing Properties	The notified chemical does not have oxidising properties	Based on the chemical structure examination.

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

Reactivity
The notified chemical has a good stability at standard temperature.
Avoid temperature above or near to the flash point during storage. Avoid contact with oxidising agent. No reaction known with water.

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

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical is not manufactured in Australia. It will be imported as a component of fragrance preparations at maximum concentration of 1% in tightly closed lacquered drums.

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

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

PORT OF ENTRY
Sydney

IDENTITY OF MANUFACTURER/RECIPIENTS
The fragrance preparations containing the notified chemical will be imported by Firmenich Ltd and will be distributed locally to other customers.

TRANSPORTATION AND PACKAGING
The fragrance preparations containing the notified chemical up to 1% will be imported in tightly closed lacquered drums, typically of 180 kg size, but also in 5, 10, 25, 50 or 100 kg packages. They will be transported by road from the wharf or airport of entry to the Firmenich Ltd warehouse for storage and then distributed to customers/manufacturers for incorporation/blending/formulation into a wide variety of cosmetics, toiletries and household products.

USE
The notified chemical will be used as a fragrance ingredient in a variety of cosmetic and domestic products. The concentration of the notified chemical in finished consumer products will be up to 1% in fine perfumes and up to 0.005% in other cosmetic and domestic products.

OPERATION DESCRIPTION
The notified chemical will not be manufactured in Australia and will be imported as a component (maximum of 1%) of compounded fragrances. The fragrance preparations containing the notified chemical will be reformulated in Australia and will be used to produce perfume cosmetics, household cleaning and detergent products.

The reformulation process mainly involves a blending operation which will be highly automated and will occur in a fully enclosed environment, followed by automatic filling in containers of various sizes. The final consumer products will be distributed to retail outlets and sold to the public. The concentration of the notified chemical in finished consumer products will be a maximum of 1% in fine perfumes and a maximum of 0.005% in other cosmetic and domestic products.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport workers	4	Unknown	unknown
Mixer	5	4	2
Drum handling	5	4	2
Drum cleaning	8	4	2
Maintenance	5	4	2
Quality control	1	0.5	1
Packaging	10	4	2
Salon workers	100	1	300

EXPOSURE DETAILS
The major occupational exposure to the notified chemical will be at the reformulation plants where the imported containers of fragrance mixtures containing the notified chemical (at a maximum of 1%) are opened and used. Workers may be exposed to fragrances containing the notified chemical during handling of the drums, weighing and charging them to the blending vessel, mixing in open vessels and also during cleaning operations, production line, and sampling or analysis tasks. Exposure via all three routes (dermal, ocular and inhalation) is anticipated to be minimal and irregular. The number and category of workers will depend on the nature of the business.

Reformulation is usually done in fully automated systems; however some facilities may not be fully automated. Hazardous components of the products mixed together as well as the size of the batches usually necessitate the

use of closed lines, local exhaust ventilation where vapours or aerosols are produced, and automated packing lines.

All workers handling perfume preparations containing the notified chemical and involved in open mixing operations will be wearing suitable gloves, eye and face protection and protective clothing. If open vessels are used for mixing, adequate ventilation will be provided to remove aerosols that may arise during the process. It is very unlikely that the product containing the notified chemical will be added to the mixing vessel manually.

Workers in hair and beauty salons will experience extensive dermal exposure during application of products containing the notified chemical at only up to 0.005% or less by hand. Such professionals may use some personal protective equipment to minimise repeated exposure, and good hygiene practices are expected to be in place. Exposure of such workers is expected to be of a similar or higher level than that experienced by consumers using products containing the notified chemical.

Overall, the exposure of these workers to the notified chemical is expected to be low.

6.1.2. Public exposure

During import, transport, storage, reformulation of fragrance compositions containing the notified chemical, exposure of the general public will be limited, except in the event of an accidental spill.

End-use products are designed to be sold to consumers. The general public will be repeatedly exposed to the notified chemical up to 1% in fine fragrance, up to 0.005% in cosmetic products and domestic products.

Public exposure to the notified chemical is expected to be widespread and frequent through daily use of personal care products containing the notified chemical. Exposure to the notified chemical will vary depending on individual use patterns. The principal route of exposure will be dermal and accidental ocular exposure may also occur. Inhalation exposure is also possible if products are applied by spray. Accidental ingestion from the use of these types of products is also possible from facial use.

Considering the very low concentrations used in consumer products (up to 0.005%), exposure to public is not considered significant.

Public exposure to the notified chemical in fine fragrances at 1% was estimated using the Scientific Committee on Consumer Products' (SCCP's) Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation using 100% dermal absorption for a 60 kg female (SCCP, 2006).

Product type	mg/event	events/day	C (%)	RF	Daily exposure (mg/day)	Body weight (kg)	Daily systemic exposure* (mg/kg bw/d)
Fine perfume	750	1	1	1	7.5	60	0.125

C = concentration; RF = retention factor; Daily exposure = mg/event x events/day x C (%) x RF;
*Daily systemic exposure = [daily exposure x dermal absorption %] / bw

The total systemic exposure was estimated as 0.125 mg/kg bw/day for a 60 kg female.

6.2. Human health effects assessment

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

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	Slight irritant with reversible effect
Rabbit, eye irritation	irritant
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Skin sensitisation – HRIPT	no evidence of sensitisation
Rat, repeat dose toxicity – 28 days.	NOAEL = 150 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro in mouse lymphoma cell	non genotoxic
Phototoxicity Human study	no effects

Toxicokinetics, metabolism and distribution.
The notified chemical data provided to describe the likely toxicokinetic properties of the notified chemical, the low molecular weight, adsorption/desorption (log K_{OC} = 2.7), and the partition coefficient (log Pow = 2.94) indicate that absorption following ingestion and dermal exposures may occur. The low vapour pressure ($9.8x10^{-5}$ kPa) of the notified chemical indicates a low inhalation exposure.

Acute toxicity.
The notified chemical was of low acute oral and dermal toxicity. No inhalation toxicity data are provided.

Irritation and Sensitisation.
The notified chemical was an eye irritant when tested undiluted on eyes of rabbit. It was slightly irritating to skin of rabbit when tested undiluted.

The notified chemical was not a sensitiser in both tests: Guinea pig "Magnusson & Kligman Maximisation" skin sensitisation adjuvant test and Skin sensitisation HRIPT test.

Repeated Dose Toxicity (sub acute, sub chronic, chronic).
The effect of repeated exposure to the notified chemical for 28 days was investigated in the rat at dose levels of 15, 150 and 1000 mg/kg/day. The only findings at 1000 mg/kg bw/day, which were considered to be indicative of toxicity, were slightly lower bodyweight gains and motor activity in males and occasional activity and abnormal gain in both sexes. Due to these findings of toxicity, the dose level of 1000 mg/kg bw/day cannot be classed as a clear NOAEL. However, a NOAEL was established as 150 mg/kg bw/day, based on the absence of statistical significance or any other findings of toxicological effects at this dose (only a slight low rearing activity in male in test versus control animals).

Mutagenicity
The notified chemical was not mutagenic in a bacterial reverse mutation test and was also not clastogenic in a mouse lymphoma cell line.

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

R36 Irritating to eyes

6.3. Human health risk characterisation

6.3.1. Occupational health and safety

The primary risk to workers from exposure to the notified chemical is eye irritation and slight skin irritation. There is a potential for dermal and ocular exposure during various processes involving the notified chemical. However, the risk of irritancy effects in workers would be reduced due to the limited exposure through use of engineering controls (exhaust ventilation), personal protective equipment (such as safety glasses, gloves and overalls) and the highly automated reformulation process which will occur in a fully enclosed environment, followed by automatic filling.

Employees in hair and beauty salons will experience extensive dermal exposure during application of products containing the notified chemical (<0.005%) by hand. If these employees use products containing the notified chemical for personal use as well as in a work setting their level of exposure would be higher than that of consumers. However, exposure to the notified chemical at low concentrations (<0.005%) is not expected to cause skin or eye irritation. The risk of toxicity following repeated exposure is not anticipated to be unacceptable.

Overall, the notified chemical is not expected to pose an unacceptable risk to workers under the occupational conditions described.

6.3.2. Public health

The public may come into contact with the notified chemical up to 1% in fine fragrances and up to 0.005% through the use of a range of cosmetic and consumer/domestic products.

The acute risk associated with the notified chemical is slight skin and eye irritation. At the proposed maximum use concentration of up to 1%, irritation effects are not expected.

Considering the very low concentration of the notified chemical in consumer/domestic products (up to 0.005%), risk from repeated exposure is not considered unacceptable.

MOE of 1200 was estimated for fine fragrance use with the systemic exposures estimated in sec.6.1.2 (0.125 mg/kg bw/d) and using a NOAEL of 150 mg/kg bw/day established in a 28-day rat study. MOE greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences.

Based on the MOE (>100), the risk from repeated use of the notified chemical in fine fragrances is considered to be acceptable.

Therefore, when used in the proposed manner, the risk to the public from the use of the notified chemical, at up to 0.005% in cosmetic /domestic products, and up to 1% in fine fragrances is not considered to be unacceptable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported as a component of fragrance preparations for local reformulation into a variety of consumer products (cosmetics, household products, fine fragrance). Losses during the blending processes at various sites throughout Australia are expected to be limited to traces of spills, formulation equipment cleaning and residues in empty packaging. Less than 0.1 % of the total annual import volume of notified chemical is expected to remain as residues in import containers. The empty containers will eventually be recycled or disposed of to landfill. At the end of the reformulation run the formulating equipment and packing equipment is washed and it is anticipated that the washings will be included in the next batch.

Accidental spills during transport or reformulation are expected to be collected with inert material and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

Most of the notified chemical will be incorporated as a fragrance additive into a variety of consumer products for dispersed use throughout Australia. Whilst there will be some releases of this moderately volatile fragrance chemical to the atmosphere, the majority of the imported quantity of notified chemical is expected to be released to the sewer in domestic situations.

RELEASE OF CHEMICAL FROM DISPOSAL

Expired wastes and residue of the notified chemical in empty containers (<0.1%) are likely either to share the fate of the container and be disposed of to landfill, or to be washed to the sewer when containers are rinsed before recycling.

7.1.2 Environmental fate

The notified chemical is a moderately volatile compound and some of the imported quantity of this chemical will partition to air, which is a functional requirement for fragment products. The half-life of the notified chemical in air was calculated to be 6.01 h, based on reactions with hydroxyl radicals over a 12 hour day, and reaction with ozone was not predicted (AOPWIN, v1.92; EPISuite, US EPA 2009). The notified chemical is therefore not expected to persist in the air compartment.

The major proportion of the imported quantity of notified chemical will enter the sewer system as a result of the use of this chemical as an odorant in domestic consumer products such as cosmetics and household products. The notified chemical did not satisfy the criteria for ready biodegradability, but the extent of biodegradation in the test (<7%) indicates a potential for biodegradation in the environment, and to some extent during sewage treatment. Some partitioning to sludge is expected based on the notified chemical's surface activity and its measured adsorption coefficient (log K_{OC} = 2.7). Most of the notified chemical is expected to remain in the water phase, due to its high water solubility, and may be released from sewage treatment plants to receiving waters, where it will disperse and slowly degrade.

It is not likely to bioaccumulate, based on its low bioconcentration factor (log BCF = 1.35) predicted by a regression-based method (BCFBAF v3.00; US EPA, 2009).

A small proportion of notified chemical may be applied to land when effluent is used for irrigation or when sewage sludge is used for soil remediation. Notified chemical residues in landfill, soil and sludge are likely to be relatively mobile, and are expected to degrade biotically or abiotically to form water and oxides of carbon.

For the details of the environmental fate studies, refer to Appendix C.

7.1.3 Predicted Environmental Concentration (PEC)

A Predicted Environmental Concentration (PEC) has been calculated assuming a worst case in which 100% of the annual imported quantity of notified chemical will be released to sewer nationwide and that no removal of the notified chemical will occur at 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)	21.161	million
Removal within STP	0%	
Daily effluent production:	4,232	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.65	µg/L
PEC - Ocean:	0.06	µg/L

The notified chemical is likely to be partially removed from STP influent due to partitioning to sludge and its potential for biodegradation. However, for this worst case scenario it is assumed that all of the notified chemical is released to the environment as STP effluent. STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 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 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.647 µg/L may potentially result in a soil concentration of approximately 4.316 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 21.58 µg/kg and 43.16 µg/kg, respectively. However, given the relative mobility of the notified chemical, and its potential for biodegradability, these concentrations should be considered as maximum values only.

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 LC50 = 14.4 mg/L	Harmful to fish
Daphnia Toxicity	48 h EC50 = 27.2 mg/L	Harmful to aquatic invertebrates
Algal Toxicity	72 h E_rC50 = 26.6 mg/L	Harmful to algae
Inhibition of Bacterial Respiration	3 h IC50 = 270 mg/L	Not inhibitory to microbe respiration

Under the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS), the notified chemical is considered to be acutely harmful to fish, daphnia and algae. Based on its acute toxicity to aquatic biota, the notified chemical is formally classified under the GHS as 'Acute Category 3; Harmful to aquatic life' and, as the notified chemical is not rapidly degradable, as 'Chronic Category 3; Harmful to aquatic life with long lasting effects'.

7.2.1 Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC) has been calculated using the endpoint for the most sensitive trophic level (fish 96 h LC50) and an assessment factor of 100, as the endpoints for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LC50 (Fish)	14.4	mg/L
Assessment Factor	100	
PNEC:	144.0	µg/L

7.3. Environmental risk assessment

Based on the above PEC and PNEC values, the following Risk Quotient (Q) has been calculated:

Risk Assessment	*PEC µg/L*	*PNEC µg/L*	*Q*
Q - River:	0.65	144	0.004
Q - Ocean:	0.065	144	0.0004

The majority of the notified chemical will be disposed of to the sewer. The notified chemical is unlikely to reach ecotoxicological significant concentrations in aquatic environments based on its annual importation quantity and the partial removal of the chemical from waste water by sorption to sewage sludge and its potential to slowly biodegrade. The notified chemical has a low potential for bioaccumulation and is unlikely to persist in surface waters. The risk quotient (PEC/PNEC) for the conservative worst case scenario of unmitigated release of the notified chemical to surface waters in treated effluents is well below 1 for both riverine and oceanic discharge scenarios. Therefore, at the maximum importation volume, the notified chemical is not expected to pose a risk to the environment when used as described.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification

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

R36 Irritating to eyes

and

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

	Hazard category	*Hazard statement*
Eye irritation	2B	Causes eye irritation
Aquatic Environment	Acute Category 3	Harmful to aquatic life
	Chronic Category 3	Harmful to aquatic life with long lasting effects

Human health risk assessment

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

When used in the proposed manner, the notified chemical is not considered to pose an unacceptable risk to public health.

Environmental risk assessment

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

Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- Safe Work Australia, should consider the following health and environmental hazard classification for the notified chemical:
  - Xi; R36 Irritating to eyes
  - R52/53 Harmful to aquatic life, Harmful to aquatic life with long lasting effects

- Use the following risk phrase for products containing the notified chemical at conc. ≥20%, Xi; R36 Irritating to eyes.

CONTROL MEASURES
Occupational Health and Safety

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

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

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

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

Disposal

- The notified chemical should be disposed of to landfill.

Emergency procedures

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

Regulatory Obligations

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

Therefore, the Director 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;

(2) Under Section 64(2) of the Act; if

- the function or use of the chemical has changed from a component of cosmetic/domestic products and for fine fragrances at concentrations more than 1% 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.

No additional secondary notification conditions are stipulated.

Material Safety Data Sheet

The MSDS of the notified chemical and products containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point 44.3°C

Method OECD TG 102 Melting Point/Melting Range.
EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks Capillary method
Test Facility RCC (2000)

Boiling Point 279°C at 97.3 kPa

Method OECD TG 103 Boiling Point.
EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks Differential scanning calorimetry (DSC)
Test Facility SPL (2000)

Density 1070 kg/m^3 at 20°C

Method OECD TG 109 Density of Liquids and Solids.
EC Directive 92/69/EEC A.3 Relative Density.
Remarks Determined using a pyknometer at 20°C.
Test Facility Huntingdon Life Sciences Ltd (2005a)

Vapour Pressure $9.8x10^{-5}$ kPa at 25°C

Method OECD TG 104 Vapour Pressure.
EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Determined using a vapour pressure balance.
Test Facility Huntingdon Life Sciences Ltd (2005a)

Water Solubility 0.609 g/L ± 0.008 g/L at 20°C ± 2°C, pH 9

Method OECD TG 105 Water Solubility/EC Directive 92/69/EEC A.6 Water Solubility. Flask Method. After a preliminary test, samples of the test substance (~0.1 g) were added to water (120 mL) in bottles protected from the light and shaken at ~30°C for 24 to 72 hours. After standing for 24 h at 20°C, the concentration of test substance in diluted aliquots were determined by HPLC (UV).
Remarks The saturated solutions were reported to be whitish in colour, and sample aliquots were not reported to be filtered before concentration analysis. Therefore, these results should be treated with caution.
The water used in the test was pH 9.12, and the test solutions were measured to be pH 9.25, 8.88, and 8.59 depending on whether the test solutions were shaken at 30°C for 24, 48 or 72 hours, respectively.
Test Facility Centre International de Toxicologie (CIT) (2000a)

Hydrolysis as a Function of pH $t_{½}$ >1 year at 25°C, pH 4-9

Method OECD TG 111 Hydrolysis as a Function of pH.
Test concentrations (200 mg/L) at pH 4, 7, and 9 were maintained at 50°C in the dark. After 5 days, samples were analysed by HPLC to determine concentrations of the test substance and hydrolysis products.

pH	*T (°C)*	*$t_{½}$ <hours or days>*
4	25	>1 year
7	25	>1 year
9	25	>1 year

Remarks Less than 10% hydrolysis was observed after 5 days at 50°C at pH 4, 7, and 9. Therefore, the test material is considered hydrolytically stable with a half life greater than 1 year at

25°C.
Test Facility Huntingdon Life Sciences Ltd (2005b)

Partition Coefficient (n-octanol/water) log K_{OW} = 2.94 at 21°C ± 2°C

Method OECD TG 117 Partition Coefficient (n-octanol/water)/EC Directive 92/69/EEC A.8 Partition Coefficient. HPLC Method. The partition coefficient was determined by interpolation from a calibration curve constructed from six known standards (log K_{OW} range 2.1 to 4.5) in accordance with the guidelines above.
Remarks Although the notified chemical has surface active characteristics, the HPLC conditions appear to be appropriate for this structure as there was no peak broadening observed.
Test Facility Centre International de Toxicologie CIT (2000b)

Adsorption/Desorption – screening test log K_{OC} = 2.7 at 25°C

Method OECD TG 121 Estimation of the Adsorption Coefficient (K_{oc}) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC). HPLC Method. The adsorption coefficient was determined by interpolation from a calibration curve constructed from known standards (log K_{oc} range 1.25 to 5.63) in accordance with the guidelines above.
Remarks Although the notified chemical has surface active characteristics, the HPLC conditions appear to be appropriate for this structure as there was no peak broadening observed. The notified chemical was determined to have a partition coefficient (log K_{OC}) of 2.7, indicating medium mobility in soil, sediment and sludge.
Test Facility Huntingdon Life Sciences Ltd (2005a)

Flash Point 142°C at 101.3 kPa

Method EC Directive 92/69/EEC A.9 Flash Point.
Remarks Closed cup equilibrium method
Test Facility SEPC (2000a)

Flammability Not highly flammable

Method EC Directive 92/69/EEC A.10 Flammability (Solids).
Remarks No ignition and no propagation of flame were observed after application of the flame. No burning rate could be measured.
Test Facility SEPC(2000b)

Autoignition Temperature >400°C

Method EC Directive 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks Refractory cylinder furnace used.
Test Facility Huntingdon Life Sciences Ltd (2005a)

Explosive Properties Not likely to be explosive

Method EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks Chemical structure examination.
Test Facility Huntingdon Life Sciences Ltd (2005a)

Surface Tension 46.5 mN/m at 20°C

Method	OECD TG 115 Surface Tension of Aqueous Solutions. EC Directive 92/69/EEC A.5 Surface Tension.
Remarks	Determined with a surface tension torsion balance. The notified chemical is considered to be surface active.
Test Facility	Huntingdon Life Sciences Ltd (2005a)

Oxidizing Properties The notified chemical does not have oxidising properties.

Method	EC Directive 92/69/EEC A.17 Oxidizing Properties (Solids).
Remarks	Chemical structure examination.
Test Facility	Huntingdon Life Sciences Ltd (2005a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical (92-99%)
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method. EC Directive 92/69/EEC B.1tris Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain	Rat/SD/ 2 groups of 3 males and 1 group of 3 females
Vehicle	Corn oil
Remarks - Method	Gavage / 200 and 2000 mg/kg doses used.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
3 males	3 M	200	0
3 males	3M	2000	1(day2)
3 females	3 F	2000	0

LD50	>2000 mg/kg bw
Signs of Toxicity	No clinical signs and no deaths were observed in the 3 males given 200 mg/kg. At 2000 mg/kg dose level, hypoactivity or sedation and piloerection were noted in all animals on day 1; dyspnea was observed in few animals and coma was recorded in two males. On day 2, one male was found dead. Hypoactivity, dyspnea and piloerection persisted in the surviving animals. No clinical signs weer observed in females. No clinical signs were observed in all surviving animals, from day 4 until the end of observation period.
Effects in Organs	No apparent abnormalities were found in the animal found dead and in the surviving animals killed at the end of the study.
Remarks - Results	The body weight gain of the males given 200 mg/kg was lower than that of CIT historical control animals between day 1 and day 8. The body weight gain of the surviving animals given 2000 mg/kg was not affected by treatment with the test substance.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Centre International de Toxicologie (CIT) (2000d)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical (92-99%)
METHOD	OECD TG 402 Acute Dermal Toxicity. EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal).
Species/Strain	Rat/SD 5 males and 5 females
Vehicle	Corn oil
Type of dressing	Semi-occlusive.
Remarks - Method	Single dermal dose at 2000 mg/kg by topical application (no control animals were included in this study)

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
5 males	5 M	2000	0
5 females	5 F	2000	0

LD50	>2000 mg/kg bw
Signs of Toxicity - Local	No dermal reactions were observed in any animal during the study.
Signs of Toxicity - Systemic	There were no deaths and no systemic response to treatment in animals.
Effects in Organs	No abnormalities were noted in any animal at the macroscopic examination at study termination on day 15.

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

TEST FACILITY Huntingdon Life Sciences Ltd. (2006a)

B.3. Irritation – skin

TEST SUBSTANCE Notified chemical (92-99%)

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

Species/Strain	Rabbit/New Zealand White
Number of Animals	3 males
Vehicle	Purified water was used in order to moisten the test substance.
Observation Period	1, 24, 48 and 72 hours after removal of the dressing and then daily until reversibility of cutaneous reactions.
Type of Dressing	Semi-occlusive.
Remarks - Method	A single dose of test substance 500 mg ground to a fine powder was applied to the closely clipped skin of one flank. The untreated skin served as control

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	1.0	0.3	0.0	2	72 hours	1 (72 hours)
Oedema	0.0	0.0	0.0	0	-	0

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

Remarks - Results	In one animal, a well defined erythma was noted on day 1, then a very slight erythma persisted up to day 5. Dryness of the skin was recorded between day 6 and day 10. In a second animal, a very slight erythma was observed on day 1 and day 2 only. No cuteneous reactions were observed in the third animal.

CONCLUSION The notified chemical was slightly irritating with reversible effect to the skin.

TEST FACILITY Centre International de Toxicologie (CIT) (2000g)

B.4. Irritation – eye

TEST SUBSTANCE Notified chemical (92-99%)

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

Species/Strain	Rabbit/New Zealand White
Number of Animals	3 males
Observation Period	1, 24, 48 and 72 hours after the administration then daily until reversibility of the ocular reactions.
Remarks - Method	A single dose of 100 mg of the test substance, ground to a fine powder, was introduced into the conjunctival sac of the left eye. The right eye served as

control.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect (hours)*	*Maximum Value at End of Observation Period (72 hours)*
	1	2	3			
Conjunctiva: redness	3.0	3.0	2.7	3	72	3
Conjunctiva: chemosis	2.3	2.7	2.3	3	48	2
Conjunctiva: discharge	0.7	1.0	0.7	2	24	0
Corneal opacity	2.0	2.0	2.0	2	72	2
Iridial inflammation	1.0	1.0	1.0	1	72	1

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

Remarks - Results

Very slight to moderate conjunctival reactions were observed in all animals from day 1 a very slight to moderate chemosis (grade 1 to 3), a very slight to moderate redness of the conjunctiva (grade 1 to 3) and a clear discharge were noted. These reactions persisted up to day 6, 10 or 11. A slight iritis (grade 1) was noted in all animals on day 2; it persisted up to day 4, 5 or 6.
A slight corneal opacity (grade 2) was recorded in all animals on day 2; a very slight or slight corneal opacity (grade 1 or 2) persisted up to day 4 (one animal) or 7. Neovascularisation was noted in one animal, from day 6 up to day 9.

CONCLUSION

The notified chemical was irritating to the eyes.

TEST FACILITY

Centre International de Toxicologie (CIT) (2000f)

B.5. Skin sensitisation

TEST SUBSTANCE

Notified chemical (92-99%)

METHOD

OECD TG 406 Skin Sensitisation - < Magnusson & Kligman Maximisation >.
EC Directive 96/54/EC B.6 Skin Sensitisation - < Magnusson & Kligman Maximisation >.

Species/Strain

Guinea-pigs/30

PRELIMINARY STUDY

No preliminary assay was performed.

MAIN STUDY

Number of Animals

Test Group: 10 males and 10 females
Control Group: 5 males and 5 females

INDUCTION PHASE

Induction Concentration:
intradermal: 5% in corn oil
topical: 50% in corn oil

Signs of Irritation

The notified chemical was shown to be non-irritant during intradermal induction. .

CHALLENGE PHASE

challenge

topical: 25% in corn oil

Remarks - Method

The sensitivity of the guinea pigs in CIT experimental conditions was checked with a positive sensitiser, Mercaptobenzothiazole. During the induction period, the reference substance was applied at the concentration of 1%, (day 1) and 20% (day 8) in corn oil. For the challenge application, the reference substance was applied at the concentration of 20% in corn oil.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: 1st challenge*	
		24 h	*48 h*
Test Group	25%	0	0
Control Group	25%	0	0

Remarks - Results: No clinical signs and no deaths were noted during the study. After the challenge application, no cutaneous reactions were observed of the control and treated groups.
Positive sensitisation response was observed in 100% animals treated with Mercaptobenzothiazole.

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

TEST FACILITY: Centre International de Toxicologie (CIT) (2000e)

B.6. Repeat dose toxicity

TEST SUBSTANCE: Notified chemical (92-99%)

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: Four groups of Crl:CD (SD)IGS BR rats of 5 males and 5 females each
Route of Administration: Oral – gavage
Exposure Information: Total exposure days: 28 days
Dose regimen: 7 days per week
Post-exposure observation period: Daily throughout the treatment period, detailed observations were performed immediately before dosing and between one and two hours after completion of dosing of all groups. A further observation was performed as late as possible in the working day during the first week of treatment.
Vehicle: 1.0% w/v methylcellulose in water
Remarks - Method: During the study, clinical condition and detailed physical observations, sensory reactivity, grip strength, motor activity, bodyweight, food consumption, haematology, blood chemistry, organ weight, macropathology and histopathology investigations were undertaken.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5 males + 5 females	0	None
low dose	5 males + 5 females	15	None
mid dose	5 males + 5 females	150	None
high dose	5 males + 5 females	1000	None

Mortality and Time to Death
There were no unscheduled deaths during the study.

Clinical Observations
Animals of both sexes receiving treatment at 1000 mg/kg bw/day were observed with low transient incidences of post-dose salivation, underactivity, abnormal gait and flat posture. Motor activity assessment revealed a slightly reduced activity (both cage floor and rearing activity) for the first half hour of the 1-hour recording period in males receiving 1000 mg/kg bw/day, whereas males at 150 mg/kg bw/day exhibited a reduced rearing activity.
Low bodyweight gain and low efficiency of food utilisation, recorded in males receiving 1000 mg/kg bw/day,

were considered to be related to treatment, whereas food consumption was considered not to be affected by treatment. Sensory activity and grip strength were considered to be unaffected by treatment for all animals.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

At the end of the treatment period, analysis of the haematological parameters for animals treated at 1000 mg/kg bw/day revealed lower than control white blood cell count for males and higher than control mean prothrombin time for animals of both sexes. Analysis of the blood chemistry parameters on this occasion revealed lower than control urea concentrations and higher than control albumin concentrations with concomitant higher albumin to globulin (A/G) ratios for animals of both sexes at 1000 mg/kg bw/d, as well as lower creatinine concentrations for females at this dose level.

Effects in Organs

In males and females at 1000 mg/kg bw/day, higher than control mean liver weights were measured, enlargement of the liver was noted at the macropathology examination and liver centrilobular hepatocyte hypertrophy was found in the majority of animals at the histopathology examination. Also, higher than control mean kidney weights were recorded for the females and lower than control mean adrenals and spleen weights were recorded for males.

Remarks – Results

Liver was identified as a target organ in this study with adaptive but not adverse treatment-related changes. There was some limited evidence that the test substance affected the functional capacity of the kidney but there were no indications of adverse effects on this organ. The only findings at 1000 mg/kg bw/day, which were considered to be indicative of toxicity, were slightly lower bodyweight gains and motor activity in males and abnormal gain in both sexes. Due to these findings of toxicity, the dose level of 1000 mg/kg bw/day cannot be classed as a clear NOAEL. No adverse effects of treatment were observed at the preceding dose level of 150 mg/kg bw/day. A difference in male rearing behaviour, slightly low rearing activity in test versus control animals, was observed at 150 mg/kg bw/day, but in the absence of statistical significance or any other findings, this activity was considered not to be of toxicological importance. Thus, 150 mg/kg bw/day can be classed as the NOAEL for this study.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established as 150 mg/kg bw/day in this study, based on a slight low rearing activity in males compared to the control group.

TEST FACILITY	Huntingdon Life Sciences Ltd. (2006b)

B.7. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical (92-99%)
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure/Pre incubation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, *E. coli*: WP2uvrA,
Metabolic Activation System	S9-mix (from a liver microsomal fraction of rats treated with Aroclor 1254).
Concentration Range in Main Test	a) With metabolic activation: 0-1500 µg/plate b) Without metabolic activation: 0-1500 µg/plate
Vehicle	Dimethylsulfoxide (DMSO)
Remarks - Method	A preliminary toxicity test was performed to define the dose levels of the notified chemical to be used for the mutagenicity study. The test substance was then tested in two independent experiments, with and without S9-mix. Both experiments were performed according to the direct plate incorporation method except for the second test with S9-mix, which was performed according to the pre-incubation Method. The selected treatment levels were: 93.75, 187.5, 375, 750 and 1500

µg/plate for all tester strains in the first experiment as well as for the WP2 uvr A strain in the second experiment. 46.875, 93.75, 187.5, 375 and 750 µg/plate for the TA 1535 and TA 100 strains in the second experiment. 23.438, 46.875, 93.75, 187.5 and 375 µg/plate for the TA 1537 and TA 98 strains in the second experiment.

The selected treatment levels were: 93.75, 187.5, 375, 750 and 1500 µg/plate for all tester strains in the first experiment as well as for the WP2 uvr A strain in the second experiment. 46.875, 93.75, 187.5, 375 and 750 µg/plate for *Salmonella typhimurium* strains in the second experiment.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	Not indicated	*S. typhimurium* ≥750 µg/plate WP2 uvr A at 1500 µg/plate	0	Negative
Present				
Test 1	Not indicated	1500 µg/plate	0	Negative
Test 2	Not indicated	≥375 µg/plate	0	Negative

Remarks - Results

Without S9-mix:
A slight to strong toxicity was induced in *Salmonella typhimurium* strains mainly at dose levels >750 µg/plate. In the WP2 uvr A strain, a slight to moderate toxicity was noted at 1500 µg/plate.
The test substance did not induce any noteworthy increase in the number of revertants in both experiments in any of the five strains.

With S9-mix:
In the first experiment, a slight to marked toxicity was noted at 1500 µg/plate.
In the second experiment, a slight to marked toxicity was induced at dose levels >375 µg/plate.
The notified chemical did not induce any noteworthy increase in the number of revertants in both experiments in any of the five strains.
The number of revertants for the vehicle and positive controls was as specified in the acceptance criteria. The dose levels of the positive controls were as follows:

Without S9 mix:
1 µg/plate of sodium azide (NaN_3): TA 1535 and TA 100 strains
50 µg/plate of 9-Aminoacridine (9AA): TA 1537 strain
0.5 µg/plate of 2-Nitrofluorene (2NF): TA 98 strain
2 µg/plate of 4-Nitroquinoline 1-oxide (4NQO): WP2 uvrA

With S9 mix:
2 µg/plate of 2-Anthramine (2AM): *S. typhimurium strain*
10 µg/plate of 2-Anthramine (2AM): *E. coli*: WP2uvrA strain

The study was therefore considered valid.

CONCLUSION

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

TEST FACILITY

Centre International de Toxicologie (CIT) (1999)

B.8. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical (92-99%)
METHOD	OECD TG 476 In vitro Mammalian Cell Gene Mutation Test. EC Directive 2000/32/EC B.17 Mutagenicity - In vitro Mammalian Cell Gene Mutation Test.
Cell Type/Cell Line	Mouse lymphoma L5178Y cell
Metabolic Activation System	S9 fraction from Aroclor 1254 induced rat liver
Vehicle	Dimethylsulphoxide
Remarks - Method	Preliminary toxicity test was performed with a 3 hour exposure to the test substance at concentrations form 3.44 to 1762.3 µg /mL in the absence and the presence of S9 mix. Relative suspension growth (RSG) values from 117% to 0% and from 101% to 0% were obtained in the absence and presence of S9 mix, respectively. A continuous exposure for 24 hours to test substance at concentrations 3.44 to 1762.3 µg /mL in the absence of S9 mix resulted in RSG values 87% to 0%. Concentrations used in the main test were based on this data.

Main test

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period (hours)*	*Harvest Time (hours)*
Absent			
Test 1	25*, 100*, 200*, 250*	3	48
Test 2	5*, 10*, 15*, 20*, 30*, 50*, 100*	24	48
Present			
Test 1	25*, 50*, 100*, 200*, 210*, 220*, 230*	3	48

*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	≥220.33	>230	Nil	Negative
Test 2	≥220.33	100	Nil	Negative
Present				
Test 1	≥220.33	450	450	Negative

Remarks - Results	The positive control, methyl methanesulphonate, induced an acceptable increase in mutation frequency and an acceptable increase in the number of small colony mutants (main mutation test 1 -3 hours treatment in the absence of S9 mix). The positive control, 3-methylcholanthrene, induced an acceptable increase in mutation frequency and an acceptable increase in the number of small colony mutants (main mutation test 1 -3 hours treatment in the presence of S9 mix). The positive control, methyl methanesulphonate, induced an acceptable increase in mutation frequency and an acceptable increase in the number of small colony mutants (main test -24 hour treatment in the absence of S9 mix).
CONCLUSION	The notified chemical was not clastogenic to Mouse lymphoma L5178Y cell treated in vitro under the conditions of the test.
TEST FACILITY	Huntingdon Life Sciences Ltd. (2005g)

B.9. Skin sensitisation – human volunteers

TEST SUBSTANCE	Notified chemical 10% in diethylphthalate (DEP)
METHOD	Occlusive human repeated insult patch test (HRIPT)
Study Design	Induction Procedure: 9 consecutive applications of the test substance Rest Period: 10-15 days Challenge Procedure: Challenge phase initiated during the sixth week of the study, with identical patches applied to sites previously unexposed to the study material. These patches were removed by subjects after 24 hours and the sites graded after additional 24 hours and 48 hours periods, i.e. , 48 and 72 hours after application.
Study Group	Individuals: 18 years of age or older; free of any systemic or dermatologic disorder; any skin type or race providing the skin pigmentation would allow discernment of erythema
Vehicle	Diethylphthalate (DEP)
Remarks - Method	116 subjects between the ages of 19 and 71 were enrolled and 107 subjects completed the study
RESULTS	
Remarks - Results	There were no adverse events reported. Under the conditions employed in this study, there was no evidence of sensitisation to the test substance at 10% in DEP
CONCLUSION	A RIPT was conducted using test substance diluted with DEP to 10% under occlusive dressing. The notified chemical was non-sensitising under the conditions of the test.
TEST FACILITY	TKL Research (2002)

B.10. Human Phototoxicity Study

TEST SUBSTANCE	Notified chemical (92-99%)
METHOD	Occlusive human patch test
Remarks - Method	22 subjects between the ages of 20 and 75 were enrolled and 21 completed the study. 0.2ml of the notified chemical was applied through to a 2 x2 cm^2 Webril pad attached to non porous, plastic film adhesive bandage. An area other than the study sites approximately 7 cm X 7 cm was divided into 6 equal sites, irradiated and underlined with a surgical marker. Xenon lamp was used as an irradiation source. The study material was applied to duplicate sites, irradiated and non irradiated sites. Approximately 24 hours after application the patches were removed. One site was irradiated with 24J/cm2 of UVA (320-400 nanometers) irradiation using a filtered light source. The other site served as a non-irradiated control. One additional area was irradiated with same irradiation using the procedure described above and served as the irradiated control. All study sites were evaluated after patch removal and 24 and 48 hours after irradiation. (ie, 48 and 72 hours after application).
RESULTS	
Remarks - Results	The notified chemical was evaluated under occlusive patch conditions to determine its ability to induce the phototoxic reaction in the skin of normal human volunteers' subjects. Fine products containing the notified chemical were evaluated. There were no adverse events reported.
CONCLUSION	Under the condition employed in this study, there was no evidence of

	phototoxicity to the notified chemical.
TEST FACILITY	TKL Research (2004)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical (92-99%)
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test.
Inoculum	Sewage sludge from a predominantly domestic sewage treatment plant
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Evolved carbon dioxide (CO_2) was trapped by barium hydroxide solution, and CO_2 concentrations were determined by acid titration. Analyses for total organic carbon (TOC) were also conducted.
Remarks - Method	In accordance with the guidelines above, the production of CO_2 of inoculated medium containing the test substance (nominally 10 mg TOC/L) was measured over 28 days. A reference (sodium acetate, 10 mg TOC/L) control and toxicity control (test substance and sodium acetate, 10 mg TOC/L each) were run in parallel. The percentage biodegradation is expressed as a ratio of evolved carbon dioxide to the initial theoretical carbon added as test substance. Test conditions were: 22°C ± 1°C, pH 7.51 to 8.8.

RESULTS

Test substance		*Sodium acetate*	
Day	*% Degradation*	*Day*	*% Degradation*
6	3.1	6	39.3
14	4.5	14	62.7
21	6.2	21	70.2
28	6.7	28	83.6

Remarks - Results

The percentage degradation of the reference compound (63%) surpassed the pass levels of 60% by 14 days and, therefore, the test is considered valid.

The difference between biodegradation values of test substance replicates slightly exceeded the recommended 20%, however as the biodegradation was very low, this was attributed to the limit of precision of the method and the low observed biodegradation test results. This deviation from protocol, is not considered to have compromised the validity of the study.

The toxicity control achieved 31% degradation by Day 14 and, as this surpasses the pass level of 25%, the test material is considered non-inhibitory to the inoculum used in the study.

The test substance achieved <7% degradation after 28 days and, as the pass levels of >60% were not reached, it is not considered to be readily biodegradable.

CONCLUSION	The notified chemical is not readily biodegradable
TEST FACILITY	Centre International de Toxicologie (CIT) (2000c)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical (92-99%)
METHOD	OECD TG 203 Fish, Acute Toxicity Test – Semi-static
Species	Rainbow trout (*Onchorhynchus mykiss*)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	176 to 210 mg $CaCO_3$/L
Analytical Monitoring	Test substance concentrations were determined by HPLC
Remarks – Method	After a range finding test, a definitive test at nominal concentrations 0.97, 2.13, 4.70, 10.3, 22.7 and 50 mg /L was conducted according to the guidelines above. The fish, 7 per test solution, were observed for mortality and sublethal responses every 24 hours. Test conditions were: 15.6-17.1°C, pH 7.94-8.50, 16 h/8 h light dark cycle, and dissolved oxygen was 89-100% of the air saturation value. Statistical values were determined using SAFEStat LD_{50} application (SAS v8.2, 1999).

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual**		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
0	<0.01	7	0	0	0	0	0
0.97	0.946	7	0	0	0	0	0
2.13	1.97	7	0	0	0	0	0
4.70	4.29	7	0	0	0	0	0
10.3	9.49	7	0	0	0	0	0
22.7	21.7	7	0	7	7	7	7
50	47.3	7	7	7	7	7	7

*Arithmetic mean of test substance concentrations in freshly prepared and expired (24 h) media

LC50	14.4 mg/L at 96 hours (95% CI: 9.49 mg/L to 21.7 mg/L)
LOEC	0.946 mg/L at 96 hours.
Remarks – Results	After 96 hours of exposure, there was no mortality in the test concentrations or control, thereby validating that test criterion. Measured temperatures slightly exceeded the range stated in the protocol (15 ± 2°C), however, this is not likely to have affected the integrity or validity of the test. Sublethal effects were observed in all solutions containing the test substance, including darkened pigmentation, coughing, nervous erratic behaviour, hyperventilation, quiescence, loss of orientation, and immobility combined with overturned orientation at the base of the test vessel. Therefore, a NOEC was not defined from the definitive study.
CONCLUSION	The notified chemical is harmful to fish
TEST FACILITY	Huntingdon Life Sciences Ltd (2005c)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical (92-99%)
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test – static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	Test substance concentrations were determined by HPLC
Remarks - Method	After a range finding test, a definitive test at nominal concentrations 4.27,

9.39, 20.7, 45.5 and 100 mg /L was conducted according to the guidelines above. Four replicates per concentration each had 5 daphnia added. The daphnia were observed for immobilisation every 24 hours over the course of the test. Test conditions were: 19.6-21.5°C, 16 h/8 h light dark cycle, pH 7.76-8.00, and dissolved oxygen was 98-107% of the air saturation value. Statistical values were determined using SAFEStat LD_{50} application (SAS v8.2, 1999).

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual**		*24 h*	*48 h*
0	<0.01	4 × 5	0	1
4.27	3.96	4 × 5	0	0
9.39	8.91	4 × 5	0	0
20.7	19.9	4 × 5	0	3
45.5	45.9	4 × 5	12	20
100	95.6	4 × 5	20	20

*Arithmetic mean of test substance concentrations in freshly prepared and expired (48 h) media

EC50	27.2 mg/L at 48 hours
NOEC	3.96 mg/L at 48 hours
Remarks - Results	After 48 hours of exposure, there was no immobility observed in the test concentrations or control, thereby validating that test criterion. At all test levels, the media were clear and colourless, with an odour that increased in intensity at the higher concentrations. Four of the daphnia exposed to concentrations of the test substance at 8.91 mg/L were floating/trapped at the surface of the medium after 48 hours, however they remained mobile. A single daphnia each at 19.9 and 45.9 mg/L were also floating but these were immobile. These effects were considered to be treatment related based on the dose response.
CONCLUSION	The notified chemical is harmful to aquatic invertebrates
TEST FACILITY	Huntingdon Life Sciences Ltd (2005d)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical (92-99%)
METHOD	OECD TG 201 Alga, Growth Inhibition Test. EC Directive 92/69/EEC C.3 Algal Inhibition Test.
Species	*Pseudokirchneriella subcapitata* (formally known as *Selenastrum capricornutum)*
Exposure Period	72 hours
Concentration Range	Nominal: 0, 4.27, 9.39, 20.7, 45.5 and 100 mg/L Actual: 0, 3.97, 8.74, 19.0, 43.6 and 96.7 mg/L* *Arithmetic mean of test substance concentrations at start and end of test
Auxiliary Solvent	None
Water Hardness	0.24 mmol Ca^{2+} and Mg^{2+}
Analytical Monitoring	Test substance concentrations were determined by HPLC. Cell densities were determined using a haemacytometer (Improved Neubauer).
Remarks - Method	After a range finding test, a definitive test at nominal concentrations 0, 4.27, 9.39, 20.7, 45.5 and 100 mg/L (in triplicate) was conducted to assess the affect of the test substance on the growth of unicellular green algae, according to the guidelines above. Test conditions were: 24.6-25.5°C, continuous illumination, pH 7.39-9.83. Statistical values were determined by using likelihood ratio method, William's test and Dunnett's test on the

arithmetic mean of the measured test substance concentrations (SAS v8.2, 1999).

RESULTS

Biomass		*Growth*	
E_bC_{50} *mg/L at 72 h*	*NOEC mg/L*	E_rC_{50} *mg/L at 72 h*	*NOEC mg/L*
14.4	3.97	26.6	3.97

Remarks - Results

The biomass in the control increased by 17-fold, thereby validating the test. Measured temperatures slightly exceeded the range stated in the protocol (23 ± 2°C), however, this is not likely to have affected the integrity or validity of the test.

At all test levels, the media were clear and colourless, with an odour that increase in intensity at the higher concentrations.

After 48 hours, at nominal test concentrations of 45.5 and 100 mg/L, cells were visibly swollen and/or ruptured. The cells appeared normal at other test concentrations.

CONCLUSION

The notified chemical is harmful to algae

TEST FACILITY

Huntingdon Life Sciences Ltd (2005e)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE

Notified chemical (92-99%)

METHOD

OECD TG 209 Activated Sludge, Respiration Inhibition Test.
EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test

Inoculum: Activated sludge from a predominantly domestic sewage treatment works

Exposure Period: 3 hours

Concentration Range: Nominal: 76 to 1216 mg/L
Actual: Not determined

Remarks – Method

In accordance with the guidelines above, inoculated media containing synthetic sewage feed and test substance at nominal concentrations of 76, 152, 304, 608 and 1216 mg/L were evaluated for their effect on respiration rates of activated sewage sludge after 3 hours. Inoculated media containing synthetic sewage feed and reference material (3,5-dichlorophenol), at concentrations of 3, 10 and 32 mg/L, and inoculum controls were run in parallel.
The inhibitory effects of the test substance and the reference substance on the respiration rates of activated sludge are expressed as percentages of the mean respiration rate of the controls. Test conditions were: 19.6 - 20.3°C, pH 7.4 - 8.2, 200 - 250 mg $CaCO_3$/L.

RESULTS

IC50: 270 mg/L at 3 hours (95% CI: 206 mg/L to 353 mg/L)

NOEC: Not reported

Remarks – Results

As the difference between the two controls was below 15% and the IC50 of the reference substance (11.7 mg/L) was between 5 and 30 mg/L, the test was considered valid.
Under the experimental conditions the 3 hour IC50 is >100 mg/L for activated sludge and, therefore, the test substance is considered as not harmful to micro-organisms in water treatment plants.

CONCLUSION	The notified chemical is not inhibitory to microbe respiration
TEST FACILITY	Huntingdon Life Sciences Ltd (2005f)

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