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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Ethyl Safrascenate

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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This notification has been conducted under the cooperative arrangement with the Office of Pollution Prevention and Toxics (OPPT), of the United States Environmental Protection Agency (US EPA). Information pertaining to the assessment of the notified chemical as conducted by the US EPA was provided to NICNAS, and where appropriate, has been used in this assessment report. The other elements of the risk assessment and recommendations on safe use of the notified chemical were carried out by NICNAS.

Ethyl Safrascenate

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, Analytical data, Impurities, 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)
None

NOTIFICATION IN OTHER COUNTRIES
USA, EU and Philippines.

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Ethyl Safrascenate (notified chemical)

ANALYTICAL DATA
Reference ^{1}H and ^{13}C NMR, IR, GC, MS and UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY >85%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20ºC AND 101.3 kPa: colourless liquid

Property	Value	Data Source/Justification
Freezing Point	<-20ºC	Measured
Boiling Point	234ºC at 97.2 kPa	Measured
Density	964 kg/m^3 at 20ºC	Measured
Vapour Pressure	7.11x10^{-3} kPa at 25ºC	Measured
Water Solubility	12 mg/L at 20 ºC and pH 5.0	Measured (EC Directive 92/69/EEC A.6, US EPA assessment)
Hydrolysis as a Function of pH	< 10% after 10 days at 40ºC and pH 2-12	Measured
Partition Coefficient (n-octanol/water)	log P_{OW} = 3.99 at 30ºC; pH unadjusted	Measured (EC Directive 92/69/EEC A.8, US EPA assessment)
Adsorption/Desorption	log K_{OC} = 2.4 at 25°C	Measured
Dissociation Constant	Not determined	No dissociable functionality
Flash Point	98±2ºC at 101.3 kPa	Measured. Classified as C1 combustible liquid (NOHSC, 2001)
Flammability	Predicted not to be flammable	Based on the flash point
Autoignition Temperature	282±5ºC	Measured
Explosive Properties	Predicted not to be explosive	Based on the structure of the notified chemical, and oxygen balance calculations
Surface Tension	58.6 mN/m at 19.5ºC - Surface active	Measured
Oxidizing Properties	Predicted not to be oxidising	Based on the structure of the notified chemical

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

Reactivity
The notified chemical is stable under normal conditions.
Avoid temperatures above or near to the flash point during storage.

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 will not be manufactured in Australia. It will be imported as a component of fragrance preparations at maximum concentration of 10%.

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
Customers of Firmenich Ltd for reformulation.

TRANSPORTATION AND PACKAGING

The fragrance preparations containing the notified chemical up to 10% 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. They will then be distributed to customers for reformulation into end use products packaged in a variety of small package sizes. They will subsequently be transported to retail outlets.

USE
The notified chemical will be used as a fragrance ingredient in a variety of cosmetic, toiletry and household products. It will be present at a maximum concentration of 1% in fine perfumes, and a maximum of 0.025% in other products.

OPERATION DESCRIPTION
The fragrance preparations containing the notified chemical (up to 10%) will be reformulated into end use products in Australia. The reformulation process typically involves blending operations that will be highly automated and enclosed and will not usually involve manual handling by workers. The final products (containing up to 1% notified chemical) will then be transferred to smaller containers typically using automated filling processes. The final consumer products will be distributed to retail outlets and sold to the public.

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
Occupational exposure to the notified chemical will mainly occur at the reformulation plants where the imported containers of fragrance mixtures containing the notified chemical (at a maximum of 10%) will be opened and used.

Dermal, ocular and inhalation exposure of workers to fragrance mixtures containing the notified chemical may occur during handling of the drums, weighing and charging to the blending vessel, mixing in open vessels (which may occur in some facilities), during cleaning operations, sampling or analysis tasks, and transfer to end-use containers. Exposure to the notified chemical is expected to be lowered by the mainly automated and enclosed processes used, and the ventilation likely to be in place and personal protective equipment expected to be used by workers (gloves, eye or face protection etc) if mixing occurs in open vessels.

Workers in hair and beauty salons may experience extensive dermal exposure during application of products containing the notified chemical at up to 0.025% by hand. Such professionals may use some personal protective equipment (such as gloves) 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.

6.1.2. Public exposure

During import, transport, storage, and reformulation, 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 0.025% in cosmetic products and household products.

Public exposure to the notified chemical is expected to be widespread and frequent particularly through daily use of personal care products and household 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 low concentrations used in personal care and household products (up to 0.025%), significant exposure is not expected from using these product types.

The worst case exposure will be from use of fine fragrances containing the notified chemical at 1%.

Skin sensitization effects cannot be ruled out from exposure to concentrations at and above 1% of the notified chemical.

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	Irritating
Rabbit, eye irritation	Slightly irritating with reversible effects
Mouse, skin sensitisation – Local lymph node assay	Evidence of sensitisation; EC3 = 32.3
Rat, repeat dose oral toxicity – 28 days.	NOAEL= 1000 mg/kg bw
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – mammalian chromosome aberration	non genotoxic

Toxicokinetics, metabolism and distribution.
Absorption of the notified chemical may occur following ingestion, inhalation, or dermal exposure considering its low molecular weight, partition coefficient (log Pow = 3.99) and water solubility (12 mg/L).

Acute toxicity.
The notified chemical is of low acute toxicity *via* the oral and dermal route.

No acute inhalation toxicity data are provided.

Irritation and Sensitisation.
The notified chemical was irritating to the skin and slightly irritating to the eyes of rabbits when tested undiluted.

The notified chemical was found to have the potential to cause skin sensitisation based on the mouse local lymph node assay conducted with concentrations up to 40%. The Ec3 was calculated to be 32.3. Concentration at 1% and above may cause skin sensitisation effects.

Repeated Dose Toxicity
Repeated exposure to the notified chemical for 28 days was investigated in the rat at dose levels of 30, 300 and 1000 mg/kg bw/day. The effects in the liver and thyroid were observed at 1000 and 300 mg/kg bw/day. Centrilobular hepatocyte enlargement of the liver was evident in animals of either sex treated with 1000 and 300 mg/kg/day. Thyroid changes identified as follicular cell hypertrophy were evident in animals of either sex treated with 1000 mg/kg bw/day or males only treated with 300 mg/kg bw/day. These effects were considered as adaptive changes to the treatment. The NOAEL was established as 1000 mg/kg bw/day, based on no adverse effects at this dose level.

Mutagenicity.
The notified chemical was not mutagenic in a bacterial reverse mutation test and in a mammalian chromosome aberration test.

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

R38 Irritating to skin
R43 May cause sensitisation by skin contact

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
Based on the available data, adverse effects associated with exposure to the notified chemical may include skin irritation and sensitisation and possibly slight eye irritation. There is potential for dermal and ocular exposure of workers to the notified chemical at concentrations up to 10% during reformulation of the notified chemical into final products (such as during transfer, mixing, cleaning and sampling). At these concentrations, the notified chemical is not expected to cause significant irritation of the eyes or skin, though sensitization effects cannot be ruled out. The risk of these effects would be further reduced by the 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 mainly automated filling processes.

Employees in hair and beauty salons will experience extensive dermal exposure during application of products containing the notified chemical (<0.025%) 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 (<0.025%) is not expected to cause skin or eye irritation or skin sensitisation.

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

6.3.2. Public health

Members of the public may make repeated contact with the notified chemical through use in fine fragrances and cosmetic and household products.

The public may experience dermal exposure to the notified chemical at up to 1% in fine fragrances and up to 0.025% through the use of a range of cosmetic and consumer/domestic products.

At the proposed maximum use concentration of up to 0.025%, irritation and sensitization effects are not expected. Fine fragrances containing 1% concentration of the notififed chemical may have potential to cause skin sensitization. Therefore, appropriate labeling is required through The National Drugs and Poisons Scheduling Committee (NDPSC) scheduling process.

Systemic exposure of the notified chemical was calculated to be 0.125 mg/kg bw/day.

Based on the NOAEL of 1000 mg/kg bw/day established in a 28-day rat study, the MOE is calculated to be 8000. 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 at up to 1% concentration is not considered to be unacceptable.

Therefore, when used in the proposed manner, the risk to the public from the use of the notified chemical, at up to 0.025% 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 fragrances). Release during reformulation in Australia is expected to arise from spills (0.1%), formulation equipment cleaning (no release estimate as cleaning water is recycled) and residues in import containers (0.1%). Accidental spills during transport or reformulation will be collected with inert material and disposed of to landfill. Import containers will either be recycled or disposed of through an approved waste management facility. Therefore, up to 0.2% of the import volume is estimated to be released to landfill as a result of reformulation in Australia.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be released to sewer in domestic situations across Australia as a result of its use in cosmetics and toiletries which are washed off the hair and skin of consumers.

RELEASE OF CHEMICAL FROM DISPOSAL

It is estimated that a maximum of 3% of the consumer product containing the notified chemical will remain in end-use containers. These will be disposed of through domestic garbage disposal and will enter landfill or be recycled.

7.1.2 Environmental fate

Following its use in Australia, the majority of the notified chemical will enter the sewer system. Whilst ester hydrolysis is expected (US EPA assessment) the provided study indicates that hydrolysis is not significant under environmental conditions. The notified chemical is not readily biodegradable (0% biodegradation in 28 days via CO_2 Headspace, OECD TG 310, US EPA assessment, measured) but up to 18% is predicted to be removed in sewage treatment plants through partial adsorption to sludge (SimpleTreat; European Commission, 2003). However, the notified chemical is not likely to bioaccumulate, based on its low molecular weight and low bioconcentration factor (predicted log BCF = 2.4, US EPA assessment). In the case of release to surface waters, the notified chemical is expected to disperse and slowly degrade, or partition into the air compartment.

The notified chemical is expected to volatilise from water (Log H = 2.09 Pa/m^3/mol, SimpleTreat; European Commission, 2003) and a significant portion of the imported quantity of the notified chemical will partition into the air compartment. The half-life of the notified chemical in air is calculated to be ≤ 1.4 h and 0.79 h, based on reactions with hydroxyl radicals and ozone respectively, over a 12 hour day (US EPA assessment, predicted). The notified chemical is therefore not expected to persist in the air compartment.

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 expected to have medium mobility, and are expected to slowly degrade to form water and oxides of carbon.

7.1.3 Predicted Environmental Concentration (PEC)

The following Predicted Environmental Concentrations (PEC) have been calculated assuming that all of the imported quantity of notified chemical will be released to sewer. Of this, an estimated 52% of the notified chemical is predicted to partition to the air compartment and a further 18% is predicted to be removed by sewage treatment plant (STP) processes through adsorption to sludge (SimpleTreat; European Commission, 2003) before discharge to surface waters on a nationwide basis.

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	70%	**Mitigation**
Daily effluent production:	4,232	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.19	µg/L
PEC - Ocean:	0.02	µg/L

Based on the Simple Treat (European Commission, 2003) modelling prediction of 18% partitioning to sludge, partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 1.165 mg/kg (dry wt). Biosolids are applied to agricultural soils, with an assumed average rate of 10 t/ha/year. Assuming a soil bulk density of 1500 kg/m^3 and a soil-mixing zone of 10 cm, the concentration of the notified chemical may approximate 8 µg/kg in applied soil. This assumes that degradation of the notified chemical occurs in the soil within 1 year from application. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated biosolids application, the concentration of notified chemical in the applied soil in 5 and 10 years may approximate 40 µg/kg and 0.08 mg/kg, respectively.

Notified chemical that is not removed from waste water during STP processes may be released to the environment in 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 0.194 µg/L may potentially result in a soil concentration of approximately 1.295 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 6.474 µg/kg and 12.95 µg/kg, respectively.

7.2. Environmental effects assessment

The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. The provided studies include acute toxicity of the notified chemical to aquatic invertebrates and algae, and inhibition of activated sludge. Details of these studies can be found in Appendix C. In addition, modelled estimates for acute fish toxicity and chronic toxicity were provided in the US EPA assessment. The modelled acute and chronic endpoints for which measured data were not provided are also included in the table below.

Endpoint	*Result*	*Assessment Conclusion*
Acute Toxicity		
Fish Toxicity	96 h LC50 = 1.3 mg/L[1]	Toxic to fish
Daphnia Toxicity	48 h EC50 = 3.1 mg/L	Toxic to aquatic invertebrates
Algal Toxicity	72 h E_rC50 = 4.1 mg/L	Toxic to algae
Chronic Toxicity		
Fish Toxicity	32 d ChV = 0.02 mg/L[1]	Very toxic to fish with long lasting effects
Daphnia Toxicity	ChV = 0.02 mg/L[1]	Very toxic to aquatic invertebrates with long lasting effects
Algal Toxicity	96 h ChV = 0.2 mg/L[1]	Toxic to algae with long lasting effects
Inhibition of Bacterial Respiration	3 h IC50 > 1000 mg/L	Not inhibitory to bacterial respiration

[1] Modelled estimate reported in the US EPA assessment.

Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) the notified chemical is toxic to fish, aquatic invertebrates and algae, and is formally classified as 'Acute Category 2: Toxic to aquatic life'.

The notified chemical is considered very toxic with long lasting effects to fish and aquatic invertebrates and toxic with long lasting effects to algae. On the basis of its chronic toxicity to fish, aquatic invertebrates and algae, and its lack of rapid degradability, the notified chemical is formally classified under the GHS as 'Chronic Category 1: Very toxic to aquatic life with long lasting effects'.

The notified chemical is considered to be not inhibitory to bacterial respiration.

7.2.1 Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) has been calculated from the estimated chronic fish toxicity of the notified chemical and an assessment factor of 50. A more conservative assessment factor of 50 is appropriate in this case as although chronic endpoints ($ChV = (LOEC \times NOEC)^{½}$) for three trophic levels were provided in the US EPA report, these chronic endpoints are not no-observed effect concentrations (NOECs).

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
ChV (Fish).	0.02	mg/L
Assessment Factor	50.00	
Mitigation Factor	1.00	
PNEC:	0.40	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:	0.19	0.4	0.486
Q - Ocean:	0.02	0.4	0.049

The risk quotient for discharge of treated effluents containing the notified chemical to riverine environments indicates a narrow safety margin as a result of the estimated chronic toxicity of this chemical. However, the notified chemical is unlikely to reach ecotoxicological significant concentrations in riverine environments based on its annual importation quantity and the partial removal of the chemical from waste water by sorption to sewage sludge and partitioning into air. The notified chemical has a low potential for bioaccumulation and is unlikely to persist in surface waters. Therefore, at the maximum annual importation volume, the notified chemical is not expected to pose a risk to the environment based on the reported use in cosmetics and household products.

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 phrases:

R38 Irritating to skin
R43 May cause sensitisation by skin contact

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*
Mildly irritating to skin	Category 3	Causes mild skin irritation
Skin sensitiser	Category 1	May cause sensitisation by skin contact
Aquatic Environment	Acute Category 2 Chronic Category 1	Toxic to aquatic life Very toxic 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 with appropriate labelling for products containing the notified chemical at 1%, 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 considered to pose an unacceptable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- Safe Work Australia, should consider the following hazard classification for the notified chemical:
  - R38 Irritating to skin
  - Xi; R43: May cause sensitisation by skin contact

- Use the following cut-off concentration for any products/mixtures containing the notified chemical:
  - Concentration ≥20% : R38, R43
  - Concentration ≥1% : R43

ACCS

- The Advisory Committee on Chemicals Scheduling (ACCS) should consider the notified chemical for listing on the SUSMP based on the results of the skin irritation and skin sensitisation (LLNA) tests.

- Products containing the notified chemical at concentrations of 1% or above available to the public must carry safety directions and warning statements on the label consistent with the following:
  - May cause allergy

Health Surveillance

- As the notified chemical is a skin sensitiser, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of skin sensitisation.

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement, where possible, the following engineering controls to minimise occupational exposure to the notified chemical as introduced at a maximum concentration of 10%:
  - Automated and enclosed processes

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced at a maximum of 10% concentration:
  - Avoid contact with skin

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced at a maximum concentration of 10%:
  - Gloves and overalls

- 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;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a component of fine perfumes at ≤1% and in other cosmetic and household products at up to 0.025%, 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 provided by the notifier was reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point <-20ºC

Method EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Test Facility Firmenich (2007a)

Boiling Point 234ºC at 97.2 kPa

Method EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks Siwoloboff method
Test Facility Firmenich (2007a)

Density 964 kg/m^3 at 20ºC

Method EC Directive 92/69/EEC A.3 Relative Density.
Remarks Oscillating density meter method
Test Facility Firmenich (2007a)

Vapour Pressure $7.11x10^{-3}$ kPa at 25ºC

Method OECD TG 104 Vapour Pressure.
EC Directive 92/69/EEC A.4 Vapour Pressure.
Test Facility Harlan Laboratories (2009b)

Water Solubility 12 mg/L at 20 ºC and pH 5.0

Method OECD TG 105 Water Solubility.
EC Directive 92/69/EEC A.6 Water Solubility.
Remarks Flask Method/Column Elution Method
Test Facility Firmenich (2007a)

Hydrolysis as a Function of pH < 10% after 10 days at 40ºC and pH 2-12

Method In-house

pH	*T (°C)*	*% Hydrolysis*
2	40	< 10%
5	40	< 10%
7	40	< 10%
8.5	40	< 10%
12	40	< 10%

Remarks 0.001M notified chemical in buffer solutions (types A, C, D, F and I: Reference Handbook of Chemistry and Physics) with 1% non-ionic surfactant. GC-FID determination at day 1, 2, 3, 8, 15, 22 and 28. Hydrolysis was <10% after 10 days at pH 2, 5, 7, 8.5 and 12, indicating the notified chemical is expected to be hydrolytically stable under environmental conditions.
Test Facility Unspecified

Adsorption/Desorption log K_{oc} = 2.4 at 25°C

Method EC Directive 92/69/EEC C.19.
OECD TG 121. Estimation of the Adsorption Coefficient on Soil and Sewage Sludge Using High Performance Liquid Chromatography (HPLC).
Remarks No reported deviations to the protocol. The notified chemical is classified to be of medium mobility (US EPA assessment). The US EPA assessment model predicted log K_{oc} = 2.8.
Test Facility Harlan Laboratories (2009d)

Flash Point 98±2ºC at 101.3 kPa

Method	EC Directive 92/69/EEC A.9 Flash Point.
Remarks	Closed cup equilibrium method use
Test Facility	Firmenich (2007a)

Autoignition Temperature 282±5°C

Method	EC Directive 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks	Flask heater used
Test Facility	Harlan Laboratories (2009a)

Explosive Properties Predicted not to be explosive

Method	EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks	Chemical structure examination and oxygen balance calculations.
Test Facility	Harlan Laboratories (2009a)

Surface Tension 58.6 mN/m at 19.5°C - Surface active

Method	OECD TG 115 Surface Tension of Aqueous Solutions.
Remarks	Concentration: 90%
Test Facility	Harlan Laboratories (2009c)

Oxidizing Properties Predicted not to be oxidising

Method	EC Directive 92/69/EEC A.17 Oxidizing Properties (Solids).
Remarks	Based on the chemical structure
Test Facility	Harlan Laboratories (2009a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 420 Acute Oral Toxicity – Fixed Dose Procedure. EC Directive 92/69/EEC B.1 bis Acute toxicity (oral) fixed dose method.
Species/Strain	Rat/SD
Vehicle	None
Remarks - Method	No significant protocol deviations

RESULTS

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

LD50	>2000 mg/kg bw
Signs of Toxicity	No signs of systemic toxicity were noted.
Effects in Organs	No abnormalities were noted at necropsy.
Remarks - Results	There were no deaths. All animals showed expected gains in bodyweight.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Safepharm Laboratories (2007a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 402 Acute Dermal Toxicity. EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal).
Species/Strain	Rat/Wistar strain
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*
I	5 M	2000	0
II	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 14.
Remarks - Results	
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	Harlan Laboratories (2009e)

B.3. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion. EC Directive 2004/73/EC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 males
Vehicle	None
Observation Period	14 days
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	1.0	2.0	2.0	2	<7 days	0
Oedema	0.7	1.0	1.0	1	<7 days	0

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

Remarks - Results	Very slight erythema was noted in all animals one hour after patch removal with very slight to well-defined erythema noted in all animals at the 24, 48 and 72-hour observations. Very slight oedema was noted in all animals at the 24 and 48-hour observations and in two animals at the 72-hour observation. Loss of skin elasticity was noted in two animals at the 72-hour observation with crust formation noted at these two animals at the 7-day observation. One animal appeared normal at the 7-day observation and the remaining two animals appeared normal at the 14-day observation.
CONCLUSION	The notified chemical is irritating to the skin.
TEST FACILITY	Safepharm Laboratories (2007b)

B.4. Irritation – eye

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion. EC Directive 2004/73/EC B.5 Acute Toxicity (Eye Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Observation Period	1, 24, 48 and 72 hours after the administration
Remarks - Method	A volume of 0.5 mL of the test material was placed into the conjunctival sac of the right eye. The left eye remained untreated and was used as the control.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect (hours)*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0.3	0.3	0.3	2	48	0
Conjunctiva: chemosis	0.0	0.0	0.0	1	24	0
Conjunctiva: discharge	0.3	0.0	0	2	48	0
Corneal opacity	0.0	0.0	0.0	0	-	0
Iridial inflammation	0.0	0.0	0.0	1	24	0

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

Remarks - Results

Minimal to moderate conjunctival irritation was noted in all animals at the one hour observation. This reduced at 24 hour and all treated eyes appeared normal at the 48-hour observation.

No corneal effects were noted. Iridial inflammation was noted in one animal one hour after treatment.

CONCLUSION

The notified chemical is slightly irritating to the eye with reversible effects.

TEST FACILITY

Safepharm Laboratories (2007c)

B.5. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 429 Skin Sensitisation: Local Lymph Node Assay

Species/Strain: Mouse/CBA/J

Vehicle: Acetone/Olive Oil, 4:1

Positive control: Hydroxycitronellal at 15% and 60% v/v in vehicle.
Isoeugenol at 5% v/v in vehicle

Remarks - Method: No significant protocol deviations

RESULTS

Concentration (% w/v)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (*vehicle control*)	47.8	-
1	38.3	0.8
5	64.2	1.3
10	58.8	1.2
20	86.8	1.8
40	188.2	3.9
Positive Control (Hydroxycitronellal)		
15%	79.9	1.7
60%	362.0	7.6
Positive Control (Isoeugenol)		
5%	274.0	5.7

Remarks - Results

The 40% concentration of test material gave an SI value of 3.9.

A dose response was observed for the 1% – 40% range of concentrations tested. The EC-3 value was calculated as 32.3

Treatment-group mean ear thickness values (days 1 and 3) did not increase by 10% or more at any tested concentration of the test or control articles. Thus primary irritation is unlikely to have affected the LLNA stimulation indices.

CONCLUSION	There was evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	Burleson Research Technologies, Inc. (BRT, 2007)

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 Han
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week Post-exposure observation period: None
Vehicle	Arachis oil BP
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5M/5F	0	0
low dose	5M/5F	30	0
mid dose	5M/5F	300	0
high dose	5M/5F	1000	0

Mortality and Time to Death

There were no deaths during the study

Clinical Observations

A reduction in bodyweight gain was evident throughout the treatment period for males treated at 1000 mg/kg bw/day, in comparison to controls. Males treated at 300 mg/kg bw/day also showed a reduction in bodyweight gain during week 4 only. Females treated with 1000 mg/kg bw/day showed a significant increase in water consumption during the treatment period. No significant body weight changes were observed in females at any dose level.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

There were no toxicologically significant changes in the haematological parameters measured.
Females treated at 1000 mg/kg/day showed an increase in alanine aminotransferse levels, in comparison to controls. No such effect was detected in males.
There were no adverse changes detected in the hormone parameters measured and no adverse effect on the stage of oestrus in treated females, in comparison to controls.

Effects in Organs

A statistically significant increase in kidney and liver weights was evident for animals of both sexes treated at 1000 mg/kg/day. In addition, a statistically significant reduction in thyroid/parathyroid weights was evident for males treated with 1000 mg/kg/day, compared to controls. Centrilobular hepatocyte enlargement was seen in animals of either sex treated with 1000 and 300 mg/kg/day.
Higher grades of severity of globular accumulations of eosinophilic material were observed in the kidney tubular epithelium of males treated with 1000 and 300 mg/kg/day. This finding is consistent with hydrocarbon nephropathy, which results from the excessive accumulation of α 2-microglobulin in renal proximal tubular epithelial cells. This effect is unique to male rats and thus is not considered relevant to human health.
THYROID: Follicular cell hypertrophy in thyroid was seen in animals of either sex treated with 1000 mg/kg/day and for males only at 300 mg/kg/day.

Remarks – Results

Oral (gavage) administration of the test material to rats for a period of twenty eight days at dose levels of up to 1000 mg/kg/day resulted in toxicologically significant effects at 1000 and 300 mg/kg/day. Effects in organs (liver, kidney and thyroid) were considered as adaptive changes by the study author. The changes observed in kidneys were not considered relevant to human health.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 1000 mg/kg bw/day in this study, based on the absence of adverse effects at this dose level.

TEST FACILITY Harlan Laboratories (2009g)

B.7. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

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

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, *E. coli*: WP2uvrA
Metabolic Activation System	S9-mix (from livers of male Sprague-Dawley rats treated orally with three consecutive daily doses of phenobarbitone/β-naphthoflavone prior to S9 preparation on Day 4).
Concentration Range in Main Test	a) With metabolic activation: 1.5-5000 µg/plate b) Without metabolic activation: 1.5-5000 µg/plate
Vehicle	Dimethylsulfoxide (DMSO)
Remarks - Method	No significant protocol deviations

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥1500 (TA100) >5000 (WP2*uvr*A)	≥1500 (TA100, TA1537) ≥500 (TA98 & TA1535) >5000 (WP2*uvr*A)	Oily precipitate at 5000 µg/plate	Negative
Test 2	-	≥1500 (TA100) ≥150 (TA98 & TA1535) ≥500 (TA1537)	Oily precipitate at 5000 µg/plate	Negative
Present				
Test 1	≥5000 (TA100) >5000 (WP2*uvr*A)	≥1500 (TA100) ≥500 (TA1535, TA98*& 1537) >5000 (WP2*uvr*A)	Oily precipitate at 5000 µg/plate	Negative
Test 2	-	≥500 (TA100 & TA1537) ≥150 (TA1535) ≥1500 (TA98*)	Oily precipitate at 5000 µg/plate	Negative

*Experimental procedure performed at later date due to insufficient growth in original experiment

Remarks - Results The vehicle (dimethyl sulphoxide) control plates gave counts of revertant colonies within the normal range.

All of the positive control chemicals (Benzo(a)pyrene and 2-Aminoanthracene) used in the test induced marked increases in the frequency of revertant colonies, both with or without metabolic activation. Thus, the sensitivity of the assay and the efficacy of the S9-mix were validated.

No toxicity was observed for *E. coli* strain WP2uvrA-. The test material was, therefore, either tested up to the maximum recommended dose level of 5000 µg/plate or the toxic limit, depending on strain type. An oily precipitate was observed at 5000 µg/plate (under an inverted microscope only), this did not prevent the scoring of revertant colonies.

No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, with any dose of the test material, either with or without metabolic activation.

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

TEST FACILITY Safepharm Laboratories (2007d)

B.8. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical

METHOD OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
EC Directive 2000/32/EC B.10 Mutagenicity - In vitro Mammalian Chromosome Aberration Test.

Cell Type/Cell Line	Human Lymphocyte
Metabolic Activation System	Phenobarbitone/β-naphthoflavone-induced rat liver (S9 homogenate)
Vehicle	Dimethyl sulphoxide
Remarks - Method	Vehicle and positive controls cyclophosphamide (CP) and mitomycin C (MMC) were used in parallel with the test material.

A preliminary toxicity study (0 to 1942 µg/mL) was performed to define the dose levels for the main test.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 7.59, 15.17*, 30.34*, 60.69*, 91.03*, 121.38, MMC 0.4*	4 h	24 h
Test 2	0*, 7.59, 15.17*, 30.34*, 60.69*, 91.03*, 121.38, MMC 0.2*	24 h	24 h
Present			
Test 1	0*, 7.59, 15.17*, 30.34*, 60.69*, 91.03*, 121.38, CP 5*	4 h	24 h
Test 2	0*, 7.59, 15.17, 30.34*, 60.69*, 91.03*, 121.38*, CP 5*	4 h	24 h

*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	≥121.38	≥91.03	Nil	Negative
Test 2	-	≥91.03	Nil	Negative
Present				
Test 1	≥121.38	>91.03	Nil	Negative
Test 2	-	≥121.38	Nil	Negative

Remarks - Results

Test 1: Haemolysis was seen in both the presence and absence of metabolic activation at ≥30.34 µg/mL at the end of treatment.

Test 2: Haemolysis was seen in both exposure groups 4-hour and 24-hour at ≥30.34 µg/mL.

In both tests:
All vehicle control cultures had frequencies of cells with chromosome aberrations within the expected range. The positive control materials induced statistically significant increases in the frequency of cells with aberrations.

A greasy/oily precipitate was observed at concentrations ≥121.38 µg/mL in the 4 hour exposure group without metabolic activation and at ≥485.5 µg/mL in the 4 hour exposure group with metabolic activation. In the 24 h continuous exposure group greasy/oily precipitate was observed at ≥242.75 µg/mL. Haemolysis was seen in the blood cultures at the end of exposure at ≥30.34 µg/mL in all exposure groups.

The test substance did not induce any significant increases in the frequency of cells with aberrations either in the absence or presence of metabolic activation.

The test material did not induce a significant increase in the numbers of polyploid cells at any dose level in all exposure groups.

CONCLUSION

The notified chemical was not clastogenic to human lymphocytes treated in vitro under the conditions of the test.

TEST FACILITY

Harlan Laboratories (2009f)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.2.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia – Static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC/UV
Remarks - Method	After a range finding test, a definitive test was conducted in accordance with the guidelines above and in compliance with GLP standards and principles. The test media were prepared in accordance with the principles of the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, (2000) for poorly soluble substances: a saturated solution of the notified chemical with 100 mg/L loading was used at dilutions 1:3.2, 1:10, 1:32, 1:100 and undiluted. As the notified chemical is a volatile substance, the test was performed using glass tubes completely filled with test medium that were tightly sealed with glass stoppers. No significant deviations to the test protocol were reported. Test conditions: 20-21ºC; pH 7.6-8.0; 6.8-8.6 O_2/L. Statistical endpoints were estimated by probit analysis.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*[1]		*24 h*	*48 h*
Dilution 1:100	n.d.	20	0	0
Dilution 1:32	0.93	20	0	0
Dilution 1:10	2.9	20	2	7
Dilution 1:3.2	9.6	20	17	20
Saturated solution (100 mg/L loading)	29	20	20	20

[1] Geometric mean
n.d. – Not determined

EC50	5.6 mg/L at 24 hours (95% CI: 4.2-7.4 mg/L) 3.1 mg/L at 48 hours (95% CI: could not be determined)
NOEC	0.93 mg/L at 48 hours
Remarks - Results	A spacing factor of 3.2 for the test concentration was justified by the observed concentration effect relation observed during preliminary testing. There was no observed immobility in the negative control and the acceptability criteria were met: therefore, the test is considered reliable. The US EPA assessment model predicted 48-h LC50 = 1.8 mg/L (toxic to aquatic invertebrates).
CONCLUSION	Toxic to aquatic invertebrates
TEST FACILITY	Harlan Laboratories (2009j)

C.2.2. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test EC Directive 92/69/EEC C.3 Algal Inhibition Test – Static
Species	*Pseudokirchneriella subcapitata* (green alga)
Exposure Period	72 hours
Concentration Range	Nominal (dilution of saturated solution, 100 mg/L loading): 1:100, 1:32, 1:10; 1:3.2, saturated solution Actual (mg/L, geometric mean): not determined, 0.8, 2.1, 7.0 and 19
Auxiliary Solvent	None
Water Hardness	24 mg $CaCO_3$/L
Analytical Monitoring	HPLC/UV
Remarks - Method	After a range finding test, a definitive test was conducted in accordance with the guidelines above and in compliance with GLP standards and principles. The test media were prepared in accordance with the principles of the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, (2000) for poorly soluble substances: a saturated solution of the notified chemical with 100 mg/L loading was used at dilutions 1:3.2, 1:10, 1:32, 1:100 and undiluted. As the notified chemical is a volatile substance, the test was performed using Erlenmeyer flasks completely filled with test medium that were tightly sealed with glass stoppers. No significant deviations to the test protocol were reported. Additional $NaHCO_3$ (carbon source) and buffering capacity was required for the test media. Test conditions: 10000 cells/mL (initial); 22ºC; pH 8.1-10. Statistical endpoints were estimated by probit analysis and compared to the control values by the Dunnett test.

RESULTS

Biomass		*Growth*	
E_bC50	*NOEC*	*E_rC50*	*NOEC*
mg/L at 72 h	*mg/L*	*mg/L at 72 h*	*mg/L*
3.0	0.8	4.1	2.1
n.d.		(95% CI: 3.8-4.4)	

n.d. – Not determined

Remarks - Results	The pH increase during the test exceeded 1.5 units: this is likely due to reduced CO_2 transfer from surrounding air due to the use of a closed test system. However, the cell growth in the control increased from initial density by more than 16 times after 72 hours, while exponential growth was sustained for the test duration, and all other validity criteria were satisfied. Therefore, the test is considered validated. The US EPA assessment model predicted 96-h EC50 = 0.21 mg/L (very toxic to algae).
CONCLUSION	Toxic to algae
TEST FACILITY	Harlan Laboratories (2009i)

C.2.3. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test. EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test
Inoculum	Sewage sludge from domestic sewage treatment plant
Exposure Period	3 hours
Concentration Range	Nominal: 10, 32, 100, 320 and 1000 mg/L
Remarks – Method	No deviations to the test protocol were reported. Test conditions: pH 7.6-8.1.
RESULTS	
IC50	>1000 mg/L
NOEC	1000 mg/L
Remarks – Results	The test item had no significant (<10%) inhibitory effect on the respiration rate of activated sludge. The validity criteria and reproducibility for positive (3,5-dichlorophenol) and negative controls, respectively, were met. Therefore, the test is considered reliable.
CONCLUSION	The notified chemical is not harmful to microbial respiration.
TEST FACILITY	Harlan Laboratories (2009h)

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