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March 2011

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Tangerinile

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.

Tangerinile

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

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Tangerinile (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 20°C AND 101.3 kPa: Colourless liquid

Property	Value	Data Source/Justification
Freezing Point	<-20°C	Measured
Boiling Point	275°C at 97.3 kPa	Measured
Density	839 kg/m^3 at 20°C	Measured
Vapour Pressure	5.5x10^{-4} kPa at 25°C	Measured
Water Solubility	1.43x10^{-3} g/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 20 days at 40°C and pH 2-12	Measured
Partition Coefficient (n-octanol/water)	log Pow = 4.41 at 30°C; pH unadjusted	Measured (OECD TG 117, US EPA assessment)
Adsorption/Desorption	log K_{oc} = 3.25 at 25°C	Measured
Dissociation Constant	Not determined	No dissociable functionalities
Flash Point	133±2°C 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	254±5°C	Measured
Explosive Properties	Predicted not to be explosive	Based on the absence of known explosophores.
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 is stable under normal conditions.
Temperatures above or near to the flash point should be avoided 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 a 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. Packages will be transported by road from the wharf or airport of entry to the Firmenich Ltd warehouse for storage and will then be distributed to customers for reformulation into end use products. End use products are packaged in a variety

of small package sizes and 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 (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. Personal protective equipment (gloves, eye and respiratory protection etc) used by workers will reduce exposure 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 of the notified chemical into final products, 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, and up to 0.025% in cosmetics 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.

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	Slightly irritating
Rabbit, eye irritation	Slightly irritating with reversible effect
Mouse, skin sensitisation – Local lymph node assay	No evidence of sensitisation up to 40% concentration
Rat, repeat dose oral toxicity – 28 days.	NOAEL = 1000 mg/kg bw
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro Chromosome Aberration	non genotoxic
Genotoxicity – in vivo mouse micronucleus test	non genotoxic

Toxicokinetics, metabolism and distribution.
Moderate absorption of the notified chemical may occur following ingestion, inhalation, or dermal exposure considering its low molecular weight, partition coefficient (log Pow = 4.41) and water solubility (1.43 mg/L).

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

Irritation and Sensitisation.
The notified chemical was a slight eye irritant when tested undiluted on the eyes of rabbit. The notified chemical was considered to be slightly irritating to the skin. Slight desquamation was observed in all three animals at the end of the observation period (7 days) during the skin irritation test. Observation did not extend beyond 7 days and the reversibility of the desquamation within the usual required observation period (14 days) could not be confirmed. The severity of the erythma/eschar was observed to increase during the 1-hour to 72-hour time points. The mean scores for this irritation were classifiable in 1/3 animals and close to classifiable (ie mean score close to 2) in 2/3 animals. It is noted that according to the GHS criteria, the notified chemical is considered to be

a mild skin irritant (Category 3), based on the mean scores for erythema/eschar in 2/3 animals (≥1.5<2.3).

The notified chemical did not induce sensitisation in a Mouse - Local lymph node assay at up to 40% concentration.

Repeated Dose Toxicity
The effect of repeated exposure to the notified chemical for 28 days was investigated in the rat at dose levels of 30, 300 and 1000 mg/kg/day. The findings included statistically significant increases in liver weight in males treated with 1000 or 300 mg/kg/day (Mean % increase was 4.636 and 4.164 respectively). Centrilobular hepatocyte enlargement of the liver was seen in relation to treatment for males treated with 1000 mg/kg/day. Such enlargement is commonly observed in rodents following the administration of xenobiotics and, in the absence of associated inflammatory or degenerative changes, may be adaptive in nature.

Higher grades of severity of extramedullary haemopoiesis of the spleen compared to controls were seen among males treated with 1000 mg/kg/day. However, only one animal disposed severity that was considered to be outside the normal range and there was no corresponding effect on the bone marrow. These effects were also associated to the changes in haematological parameters consistent with haemolytic anaemia particularly in males treated at 1000 mg/kg/day, but also to a lesser extent in males at 300 mg/kg/day.

Mutagenicity.
The notified chemical was not mutagenic in a bacterial reverse mutation test and was not clastogenic in an in vitro Chromosome Aberration test or an in vivo mammalian erythrocyte micronucleus test.

Health hazard classification
Based on the data provided, the notified chemical cannot be classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

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 slight skin and 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. 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.

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 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.

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

At the proposed maximum use concentration of up to 1%, irritation effects are not expected.

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

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 and cosmetic and household products 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 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 consumer cosmetic and toiletries products that will be washed off the hair and skin.

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. The provided study indicates that hydrolysis is not significant under environmental conditions. Whilst the notified chemical is not readily biodegradable, it is classified as inherently degradable (61% in 28 days, OECD TG 301F, US EPA assessment, measured; C.1.1 Appendix C). Up to 17% is predicted to be removed in sewage treatment plants through partial adsorption to sludge (SimpleTreat; European Commission, 2003). The notified chemical is not likely to bioaccumulate, based on its low molecular weight and low bioconcentration factor (log BCF = 1.2, US EPA assessment, predicted). 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 = 1.84 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 2.0 h and 2.1 h, based on reactions with hydroxyl radicals and ozone, respectively (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 low mobility, and are expected to slowly degrade to form water and oxides of carbon and nitrogen.

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 41% of the notified chemical is predicted to partition to the air compartment, 18% is predicted to degrade, and a further 17% 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 nation wide 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	76%	**Mitigation**
Daily effluent production:	4,232	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.16	µg/L
PEC - Ocean:	0.02	µg/L

Based on the Simple Treat (European Comission, 2003) modelling prediction of 17% partitioning to sludge, partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 1.101 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 7 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 35 µg/kg and 70 µg/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 0.155 µg/L may potentially result in a soil concentration of approximately 1.036 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 5.179 µg/kg and 10.36 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 fish and daphnia toxicity were provided in the US EPA assessment. The modelled acute and chronic endpoints for which measured data were not provided are included in the table below.

Endpoint	*Result*	*Assessment Conclusion*
Acute Toxicity		
Fish Toxicity	96 h LC50 = 0.79 mg/L[1]	Very toxic to fish
Daphnia Toxicity	48 h EC50 = 0.17 mg/L	Very toxic to aquatic invertebrates
Algal Toxicity	72 h E_rC50 = 0.07 mg/L	Very toxic to algae
Chronic Toxicity		
Fish Toxicity	ChV = 0.097 mg/L[1]	Toxic to fish with long lasting effects
Daphnia Toxicity	ChV = 0.11 mg/L[1]	Harmful to aquatic invertebrates with long lasting effects
Algal Toxicity	NOEC = 0.03 mg/L	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 very toxic to fish, aquatic invertebrates and algae, and is formally classified as 'Acute Category 1: Very toxic to aquatic life'.

The notified chemical is considered toxic with long lasting effects to fish and algae and harmful with long lasting effects to aquatic invertebrates. On the basis of its chronic toxicity to fish, aquatic invertebrates and algae, and its rapid degradability (based on biodegradability, volatility and half life in air), the notified chemical is formally classified under the GHS as 'Chronic Category 2: 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 chronic algae 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 the other two trophic levels were provided in the US EPA assessment, these predicted chronic endpoints are not no-observed effect concentrations (NOECs).

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
NOEC (Alga).	0.03	mg/L
Assessment Factor	50	
PNEC:	0.60	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	0.6	0.259
Q - Ocean:	0.02	0.6	0.026

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 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, biodegradation 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 cannot be classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

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***
Mild Irritant	Category 3	Causes mild skin irritation
Aquatic Environment	Acute Category 1 Chronic Category 2	Very toxic to aquatic life 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, 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

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 for formulation:
  - Avoid contact with skin

- 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 up to 1% and 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 OECD TG 102 Melting Point/Melting Range.
EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Test Facility Firmenich (2008)

Boiling Point 275ºC at 97.3 kPa

Method OECD TG 103 Boiling Point.
EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks Siwoloboff method
Test Facility Firmenich (2008)

Density 839 kg/m^3 at 20ºC

Method OECD TG 109 Density of Liquids and Solids.
EC Directive 92/69/EEC A.3 Relative Density.
Remarks Oscillating density meter
Test Facility Firmenich (2008)

Vapour Pressure $5.5x10^{-4}$ kPa at 25ºC

Method OECD TG 104 Vapour Pressure.
EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Gas saturation method
Test Facility Harlan Laboratories (2009a)

Water Solubility $1.43x10^{-3}$ g/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 Harlan Laboratories (2008)

Hydrolysis as a Function of pH < 10% after 20 days at 40ºC and pH 2-12

Method In-house

pH	*T (°C)*	*% Hydrolysis at 20 days*
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, 5, 8, 15, 22 and 28. Hydrolysis was <10% after 20 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} = 3.25 at 25°C

Method	EC Directive 92/69/EEC C.19 Estimation of Adsorption Coefficient on soil using HPLC. 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 low mobility (McCall et al., 1980). The US EPA assessment model predicted K_{OC} = 3.28.
Test Facility	Harlan Laboratories (2009b)

Flash Point 133±2ºC at 101.3 kPa

Method	EC Directive 92/69/EEC A.9 Flash Point.
Remarks	Closed cup equilibrium method
Test Facility	Firmenich (2008)

Autoignition Temperature 254±5ºC

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

Explosive Properties Predicted not to be explosive

Method	EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks	Chemical structure examination
Test Facility	Harlan Laboratories (2009c)

Oxidizing Properties Predicted not to be oxidising

Method	EC Directive 92/69/EEC A.17 Oxidizing Properties (Solids).
Remarks	Chemical structure examination.
Test Facility	Harlan Laboratories (2009c)

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	1F	300	0
II	1F	2000	0
III	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 (2008a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical (purity >85%)
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 15.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	Harlan Laboratories (2009d)

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	7 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	1.7	2	7 days	0 (slight desquamation observed)
Oedema	0.3	1.0	0.7	1	7 days	0 (slight desquamation observed)

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

Remarks - Results	Very slight erythema was noted in two animals. *24 hour observation:* Well-defined erythema and very slight oedema in one animal. *48 hour observation:* Very slight erythema on one other animal *72 hour observation:* Well defined erythma and very slight oedema in two animals. Very slight erythema noted in the remaining animals. Well defined erythema and very slight oedema in all animals. Loss of skin elasticity was also noted in two animals. Slight desquamation was noted in all animals on day 7. Reversibility of the desquamation within the usual required 14 day observation could not be confirmed as the test was completed at the 7 day observation. The severity of the erythema/eschar was observed to increase during the 1-hour to 72-hour time points. The mean scores for this irritation were classifiable in 1/3 animals and close to classifiable (ie mean score close to 2) in 2/3 animals.
CONCLUSION	The notified chemical is slightly irritating to the skin.
TEST FACILITY	Safepharm Laboratories (2008f)

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	No significant protocol deviations

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			

Conjunctiva: redness	0.3	0.3	0.3	2	48 hour	0
Conjunctiva: chemosis	0.3	0.0	0.0	1	48 hour	0
Conjunctiva: discharge	0	0	0	2	24 hour	0
Corneal opacity	0.0	0.0	0.0	0	0	0
Iridial inflammation	0.0	0.0	0.0	0	24 hour	0

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

Remarks - Results
No corneal effects were noted during the study.
Iridial inflammation was noted in one animal one hour after treatment.
Moderate conjunctival irritation was noted in all animals one hour after treatment with minmal conjunctival irritation noted at the 24-hour observation. All treated eyes appeared normal after the 48-hour observation.

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

TEST FACILITY
Safepharm Laboratories (2008b)

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 (AOO)
Positive control: Hydroxycitronellal at 15% and 60% v/v in vehicle (AOO).
Isoeugenol at 5% v/v in vehicle (AOO)
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*)	13.2	-
1	23.0	1.7
5	19.1	1.5
10	18.8	1.4
20	27.9	2.1
40	35.3	2.7
Positive Control (Hydroxycitronellal)		
15%	48.9	3.7
60%	212.9	16.2
Positive Control (Isoeugenol)		
5%	213.8	16.3

Remarks - Results
The notified chemical did not cause a stimulation index of 3 or greater at any of the tested concentrations. Thus it was not considered to be a sensitizer at concentrations up to 40%

CONCLUSION
There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical under the conditions and concentrations used in this 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
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

No clinically signs of toxicity were detected.

There were no treatment-related changes in the behavioural parameters and no toxicologically significant changes in the functional performance parameters measured.

There were no treatment-related changes in sensory reactivity.

Body weight gain was not affected by treatment.

Males treated with 1000 mg/kg/day showed an increase in water consumption throughout the treatment period.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Males treated with 1000 mg/kg/day showed a haemolytic anaemia characterised by reductions in haemoglobin, erythrocyte count, haematocrit, mean cell haemoglobin concentration and an increase in reticulocyte count. A similar effect was also evident in 300 mg/kg/day males albeit to a lesser extent, with decreases in haemoglobin and haematocrit observed.

Effects in Organs

Males treated with 1000 or 300 mg/kg/day showed a statistically significant increase (Mean % were 4.636 and 4.164 respectively) in absolute liver weights. Centrilobular hepatocyte enlargement was observed in males treated with 1000 mg/kg/day, but there were no inflammatory or degenerative changes.

Higher grades of severity of extramedullary haemopoiesis compared to controls were observed in spleen of males treated with 1000 mg/kg/day. Only one animal showed severity that was considered to be outside the normal range and there was no corresponding effect on the bone marrow. This may be related to the haemolytic anaemia, as suggested by various haematology parameters.

Remarks – Results

Treatment related effects were observed in males treated with 1000 and 300 mg/kg/day. The changes in males at 1000 mg/kg/day included adaptive microscopic liver changes with associated increased liver weights. In addition, microscopic spleen changes associated with a slight anaemia were observed in males at 1000 mg/kg/day with some haematology parameters affected at 300 mg/kg/day, no dose response observed. These changes were not considered as adverse effects by the study authors.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established as 1000 mg/kg bw/day in this study, based on some haematology/ effects seen in male rats at this dose level.

TEST FACILITY	Harlan Laboratories (2009e)

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: 5-5000 µg/plate b) Without metabolic activation: 5-5000 µg/plate
Vehicle	Dimethylsulfoxide (DMSO)
Remarks - Method	Additional dose levels (5 and 15 µg/plate) were included for the *Salmonella* strains (compared to the *E. coli* strains) to allow for test material induced toxicity, ensuring that at least four non-toxic doses were achieved.

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)	≥5000	Nil	Negative
Test 2	-	≥5000	Nil	Negative
Present				
Test 1	≥1500 (TA100) >5000 (WP2*uvr*A)	≥1500	Nil	Negative
Test 2	-	≥1500	Nil	Negative

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 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 S9.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Harlan Laboratories (2009h)

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	Chinese Hamster Lung (CHL)
Metabolic Activation System	Phenobarbitone/β-naphthoflavone-induced rat liver (S9 homogenate)
Vehicle	Dimethyl sulphoxide (DMSO)
Remarks - Method	Duplicate vehicle and positive controls (Mitomicyn C (MMC) and Cyclophosphamide (CP)) were included in parallel in both experiments. No significant protocol deviations.

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 3.5, 7.0*, 14.0*, 28.0*, 35.0, MMC 0.15*	6 h	24 h
Test 2	0*, 3.5, 7.0*, 14.0*, 28.0*, 42.0, 56.0, MMC 0.075*	24 h	24 h
Present			
Test 1 (with 5% S9)	0*, 28.0, 56.0*, 84.0*, 112.0*, 196.0, CP 7.5*	6(18) h	24 h
Test 2 (with 2% S9)	0*, 28.0*, 56.0*, 84.0*, 112.0, 140.0, 168.0, CP 5*	6(18) 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	>28	≥35.0	-	Negative
Test 2	≥56.0	>28.0	-	Negative
Present				
Test 1	≥56.0	>112	-	Negative
Test 2	-	>84	-	Negative

Remarks - Results The vehicle (DMSO) controls had frequencies of cells with aberrations within the range expected for the CHL cell line.
All positive control materials induced statistically significant increases in the frequency of cells with aberrations indicating the satisfactory performance of the test method. The test material was shown to be toxic to CHL cells in vitro and optimal levels of toxicity were achieved in all exposure groups. The test material did not induce any statistically significant increases in the frequency of cells with structural or numerical aberrations in any of the exposure groups.

CONCLUSION The notified chemical was not clastogenic to Chinese Hamster Lung cell treated in vitro under the conditions of the test.

TEST FACILITY Safepharm Laboratories (2008d)

B.9. Genotoxicity – in vivo

TEST SUBSTANCE Notified chemical

METHOD OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
EC Directive 2000/32/EC B.12 Mutagenicity - Mammalian Erythrocyte

	Micronucleus Test.
Species/Strain	Albino Crl:CD-1 (ICR) BR mice
Route of Administration	Oral – gavage
Vehicle	Arachis oil
Remarks - Method	A preliminary test was performed to determine suitable test conditions. No significant protocol deviations.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	2x7M	0	24 & 48 h
II (low dose)	7M	500	24 h
III (mid dose)	7M	1000	24 h
IV (high dose)	2x7M	2000	24 & 48 h
V (positive control, CP)	5M	50	24 h

CP=cyclophosphamide.

RESULTS

Doses Producing Toxicity	≥1000 mg/kg bw
Genotoxic Effects	None
Remarks - Results	No mortality was observed. Clinical signs were observed in animals dosed at and above 1000 mg/kg bw in both 24 and 48-hour groups such as hunched posture, ptosis, ataxia and lethargy. A small but statistically significant decrease in the PCE/NCE ratio was observed in the 48-hour group compared to the control group. This, together with the observed clinical signs, suggested that systemic absorption occurred and the bone marrow had been reached. There was no evidence of a statistically significant increase of micronucleated polychromatic erythrocytes in animals dosed with the test material when compared to the vehicle control groups. The positive control groups showed a marked increase in the incidence of micronucleated polychromatic erythrocytes hence confirming the sensitivity of the test system.
CONCLUSION	The notified chemical was not clastogenic under the conditions of this in vivo Mammalian Erythrocyte Micronucleus Test.
TEST FACILITY	Safepharm Laboratories (2008c)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry.
Inoculum	Activated sewage sludge from a predominantly domestic sewage treatment plant
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Oxygen consumption
Remarks - Method	In accordance with the guidelines above, the dissolved oxygen uptake of inoculated media containing the test substance at 100, 46 and 22 mg/L, in 500 mL Erlenmeyer flasks containing 250 mL and stored in the dark, was measured over 28 days. A reference control (sodium benzoate, 100 mg/L) and a toxicity control (sodium benzoate and test substance, 100 mg/L each) were run in parallel. Biodegradation is expressed as the percentage oxygen uptake, corrected for the blank and considering complete nitrification, of the theoretical oxygen demand ($ThOD_{NO3}$). Test conditions were: 22±1°C, pH 7.2-7.8.

RESULTS

Test substance				*Sodium benzoate*	
Day	*% Degradation*			*Day*	*% Degradation*
	100 mg/L	*46 mg/L*	*22 mg/L*		
7	50	48	37	7	81
14	74	71	59	14	89
21	87	81	64	21	89
28	91	87	72	28	92

Remarks - Results

The reference control achieved >60% degradation by Day 14, and therefore the test is considered valid for this criterion. The toxicity control achieved 79% 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 oxygen uptake of the inoculum blank did not exceed 60 mg O_2/L and the pH was inside the range 6.5-8.0. Therefore, test is considered valid.

The test substance achieved at least 72% degradation after 28 days. However, the pass level of >60% within the 10-day window was not reached for all tested concentrations and, as the results are equivocal, the notified chemical is not considered to be readily biodegradable. Additionally, as the summary report did not confirm that the inoculum was not preconditioned, these results should be treated with caution. Biodegradation above 70% indicates inherent degradation of the notified chemical.

CONCLUSION	The notified chemical is inherently biodegradable
TEST FACILITY	Safepharm Laboratories (2008e)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test – Semi-static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	GC-FID
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 50 mg/L loading was used at dilutions reported above. The test was conducted in 250 mL covered (unspecified material) glass jars containing 200 mL of test preparation. Test media was renewed after 24 hours. No significant deviations to the test protocol were reported. Test conditions: 20-22ºC; pH 7.8-8.0; 8.3-8.7 mg 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*
Control	Not determined	2×10	0	0
0.039	0.026	2×10	0	0
0.070	0.058	2×10	0	1
0.12	0.090	2×10	0	0
0.22	0.26	2×10	8	16
0.39	0.36	2×10	13	20

[1] Time weighted mean

EC50	0.17 mg/L at 48 hours (95% CI: 0.15-0.19 mg/L)
NOEC	0.090 mg/L at 48 hours
Remarks - Results	The test substance was found to be unstable in the test medium thus it was justifiable to base the results on the time weighted test concentrations. After 48 hours, immobility or sub-lethal effects were not observed in the control, and other validation criteria were satisfied. The US EPA assessment model predicted 48-h LC50 = 0.65 mg/L (very toxic to aquatic invertebrates).
CONCLUSION	Very toxic to aquatic invertebrates
TEST FACILITY	Harlan Laboratories (2010)

C.2.2. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test. – Static
Species	*Desmodesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal (dilutions of saturated solution with 50 mg/L loading): 0.061, 0.18, 0.49, 1.4, 4.1 mg/L Actual (geometric mean): 0.017, 0.030, 0.049, 0.083, 0.14 mg/L
Auxiliary Solvent	None
Water Hardness	0.15 mmol Ca^{2+} and Mg^{2+}
Analytical Monitoring	GC-FID
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 50 mg/L loading was used at dilutions reported above. The test was conducted in 250 mL flasks containing 100 mL of test preparation and plugged with polyurethane foam bungs. Test conditions: $4.21x10^3$ cells/mL (initial); 24ºC±1ºC; pH 7.2-7.9. Statistical endpoints were estimated by one way analysis of variance incorporating Bartlett's test for homogeneity of variance 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*
0.033	0.017	0.070	0.030
(95% CI: 0.031-0.035)		Not determined	

Remarks - Results	A significant decline in concentration of the notified chemical was observed and the geometric mean was used to determine the endpoint. The validity criteria were satisfied. The US EPA assessment model predicted 96-h EC50 = 0.93 mg/L (very toxic to algae).
CONCLUSION	Very toxic to algae
TEST FACILITY	Harlan Laboratories (2009f)

C.2.3. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 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 Actual: Not determined
Remarks – Method	No significant deviations to the test protocol were reported. Test conditions: pH 7.2-8.0; 2.4-8.6 mg O_2/L.
RESULTS	
IC50	> 1000 mg/L
NOEC	71 mg/L
Remarks – Results	The validity criteria and reproducibility for positive (3,5-dichlorophenol) and negative controls, respectively, were met: therefore, the test is considered reliable.
CONCLUSION	Not expected to be harmful to microbial respiration
TEST FACILITY	Harlan Laboratories (2009g)

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