File No: LTD/1707

February 2014

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Cyclopentanepropanol, α,α-dimethyl-

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 conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment.

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

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

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Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/1707	Firmenich Pty Ltd	Cyclopentanepropanol, α,α-dimethyl-	YES	≤ 1 tonne per annum	Fragrance ingredient

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the table below.

Hazard classification	*Hazard statement*
Eye Irritation (Category 2A)	H319 – Causes serious eye irritation

Based on the available information, the notified chemical is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrase:

R36: Irritating to eyes.

The environmental hazard classification according to the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) is presented below. Environmental classification under the GHS is not mandated in Australia and carries no legal status but is presented for information purposes.

Hazard classification	*Hazard statement*
Acute Category 3	H402 - Harmful to aquatic life
Chronic Category 3	H412 - Harmful to aquatic life with long lasting effects

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

When used in the proposed manner, the notified chemical is not considered to pose an unreasonable 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 unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Eye irritation (Category 2A): H319 – Causes serious eye irritation

The above should be used for products/mixtures containing the notified chemical, if applicable, based on the concentration of the notified chemical present and the intended use/exposure scenario.

- The Delegate (and/or the Advisory Committee on Chemicals Scheduling) should consider the notified chemical for listing on the SUSMP.

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following isolation and engineering controls to minimise occupational exposure to the notified chemical during reformulation processes:
  - Enclosed, automated processes, where possible

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical during reformulation processes:
  - Avoid contact with eyes
  - In case of contact with eyes, rinse immediately with plenty of water and seek medical advice

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical during reformulation processes:
  - Goggles/ safety glasses with side shields

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Disposal

- The notified chemical should be disposed of to landfill.

Storage

- The handling and storage of the notified chemical should be in accordance with the Safe Work Australia Code of Practice for *Managing Risks of Hazardous Chemicals in the Workplace* (SWA, 2012) or relevant State or Territory Code of Practice.

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;
- the notified chemical is proposed to be used in fine fragrances or household products at a concentration exceeding 1%;
- the notified chemical is proposed to be used in cosmetics and toiletries at a concentration exceeding 0.5%.

or

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

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

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

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
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: other names, molecular formula, structural formula, analytical data, degree of purity, impurities, additives/adjuvants and use details.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: adsorption/desorption.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None.

NOTIFICATION IN OTHER COUNTRIES
None.

2. IDENTITY OF CHEMICAL

CAS NUMBER
83926-74-3

CHEMICAL NAME
Cyclopentanepropanol, α,α-dimethyl-

MOLECULAR WEIGHT
< 500 Da

ANALYTICAL DATA
Reference NMR, IR, GC, UV spectra were provided.

3. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	2 ± 0.5 °C	Measured
Boiling Point	208 ± 0.5 °C at 97.4 kPa	Measured
Density	0.892 kg/m^3 at 20 °C	Measured
Vapour Pressure	0.006 kPa at 20 °C 0.012 kPa at 25 °C	Measured
Water Solubility	0.461 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	No hydrolysable functionality
Partition Coefficient (n-octanol/water)	log Pow = 3.52 at 20 °C	Measured
Surface tension	44.2 mN/m at 20 °C	Measured
Adsorption/Desorption	log K_{oc} = 1.92-2.44 at 20 °C	Calculated (using KOCWIN v2.00; US EPA, 2009)
Dissociation Constant	Not determined	No dissociable functionality
Flash Point	90 ± 2 °C at 101.325 kPa	Measured
Autoignition Temperature	260 °C	Measured

Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties.
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties.

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

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

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard classification	***Hazard statement***
Flammable Liquids (Category 4)	H227 – Combustible liquid

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. The notified chemical will be imported into Australia as a component (≤ 10%) of compounded fragrances.

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, by wharf or airport.

IDENTITY OF MANUFACTURER/RECIPIENTS
Firmenich Limited.

TRANSPORTATION AND PACKAGING
The notified chemical (≤ 10% concentration) will be imported into Australia in lacquered drums of typically 180kg size, but the use of smaller containers down to 5kg is also possible. The products containing the notified chemical will be transported from the port of entry by road to the notifier's warehouse facilities for storage and then distributed to reformulation sites. The end-use products (≤ 1% notified chemical) will be packaged in containers suitable for retail sale.

USE
The notified chemical will be used as a fragrance component in a variety of cosmetic, toiletries and household products. Household products containing the notified chemical are expected to include all purpose cleaners, hard surface wipes, bleach, furniture/window cleaner, dish wash and lavatory care. The content in the final consumer products will vary, with the proposed usage concentrations of ≤ 1% in fine fragrances and household cleaning products and ≤ 0.5% in both rinse-off and leave-on cosmetic products including hair spray.

OPERATION DESCRIPTION
The notified chemical will not be manufactured within Australia. The notified chemical may be imported at ≤ 10% concentration for reformulation into cosmetic and household products containing the notified chemical at a concentration of ≤ 1%.

After the notified chemical has been imported it will be sold to cosmetic and household product manufacturers where it will be reformulated to produce a variety of cosmetic (both rinse-off and leave-on) and household products.

Reformulation
The procedures for incorporating the imported fragrance preparations (containing ≤ 10% notified chemical) into end-use products will likely vary depending on the nature of the cosmetic and personal care/household products being formulated, and may involve both automated and manual transfer steps. However, in general, it is expected that the reformulation processes will involve blending operations that will be highly automated and occur in enclosed environments. After being reformulated, the finished products containing the notified chemical (≤ 1% concentration) will be transferred via automated filling into typical consumer-sized retail packaging.

End use
The finished products containing the notified chemical may be used by consumers and may also be used in occupational settings by professionals such as hairdressers, beauticians or cleaners. Depending on the nature of the product, these could be applied in a number of ways, such as by hand, using an applicator or sprayed.

5. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport workers	unspecified	unspecified
Mixer	4	2
Drum Handling	4	2
Drum Cleaning	4	2
Maintenance	4	2
Quality Control	0.5	1
Packaging	4	2
Hairdressers/beauticians/cleaners	unspecified	unspecified

EXPOSURE DETAILS
Transport and storage workers may come into contact with the notified chemical, as a component of the imported fragrance preparations (≤ 10% concentration) or end-use products (≤ 1% concentration), only in the event of accidental rupture of containers.

During reformulation of the notified chemical into the final consumer products, dermal, ocular and inhalation exposure of workers (at ≤ 10% concentration) may occur during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. The notifier claims this exposure is expected to be minimised due to the likely use of automated processes and PPE by workers. The notifier suggests operators will wear safety glasses with shields, gloves, protective clothing, and with respiratory protection available if required.

Exposure to the notified chemical in end-use products (at ≤ 1% concentration) may occur in professions where the services provided involve the application of cosmetic and personal care products to clients (e.g. hair dressers, workers in beauty salons) or the use of household products in the cleaning industry. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible. Such professionals may use some PPE to minimise repeated exposure, but use is not expected. However, good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified chemical.

6.1.2. Public Exposure

There will be diffuse and repeated exposure of the public to the notified chemical (at ≤ 1% concentration) through the widespread use of household products and both rinse-off and leave-on cosmetic and personal care products. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray.

Data on typical use patterns of cosmetic product categories in which the notified chemical may be used are shown in the following table (SCCS, 2012; Cadby *et al*., 2002). For the purposes of the exposure assessment, Australian use patterns for the various product categories are assumed to be similar to those in Europe. An adult bodyweight of 60 kg was used for calculation purposes. Based on the (limited) dermal absorption data available on the notified chemical, a dermal absorption of 100% was assumed for the notified chemical.

- Cosmetic products (Dermal exposure):

Product type	**Amount** (mg/day)	**C** (%)	**RF** (unitless)	**Daily systemic exposure** (mg/kg bw/day)
Body lotion	7820	0.5	1	0.65
Face cream	1540	0.5	1	0.13
Hand cream	2160	0.5	1	0.18
Fine fragrances	750	1.0	1	0.13
Deodorant spray	1430	0.5	1	0.12
Shampoo	10460	0.5	0.01	0.01
Conditioner	3920	0.5	0.01	0.00
Shower gel	18670	0.5	0.01	0.02
Hand soap	20000	0.5	0.01	0.02
Hair styling products	4000	0.5	0.1	0.03
Total				1.28

C = concentration (%); RF = retention factor.
Daily systemic exposure = (Amount × C × RF × dermal absorption)/body weight

- Household products (Indirect dermal exposure - from wearing clothes):

Product type	**Amount** (g/use)	**C** (%)	**Product Retained (PR)** (%)	**Percent Transfer (PT)** (%)	**Daily systemic exposure** (mg/kg bw/day)
Laundry liquid	230	1	0.95	10	0.04
Fabric softener	90	1	0.95	10	0.01
Total					0.05

Daily systemic exposure = (Amount × C × PR × PT × dermal absorption)/body weight

- Household products (Direct dermal exposure):

Product type	**Frequency** (use/day)	**C** (%)	**Contact Area** (cm^2)	**Product Use C** (g/cm^3)	**Film Thickness** (cm)	**Time Scale Factor**	**Daily systemic exposure** (mg/kg bw/day)
Laundry liquid	1.43	1	1980	0.01	0.01	0.007	0.0003
Dishwashing liquid	3	1	1980	0.0093	0.01	0.03	0.0027
All-purpose cleaner	1	1	1980	1	0.01	0.007	0.023
Total							0.026

Daily systemic exposure = (Frequency × C × Contact area × Product Use Concentration × Film Thickness on skin × Time Scale Factor x dermal absorption)/body weight

- Cosmetic products (Inhalation exposure):

Product type	**Frequency** (use/day)	**Amount** (g/use)	**C** (%)	**Inhalation rate** (m^3/day)	**Exposure duration** (mins)	**Airspace volume** (m^3)	**Daily systemic exposure** (mg/kg bw/day)
Hairspray	2	10	1	23	15	2	0.40

Daily systemic exposure = (Frequency × Amount × C × Inhalation rate × Exposure duration × bioavailability via the inhalation route)/(body weight × Airspace volume)

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above tables that contain the notified chemical. This would result in a combined internal dose of 1.756 mg/kg bw/day. It is acknowledged that inhalation exposure to the notified chemical from use of other cosmetic and household products (in addition to hair spray) may occur. However, it is considered that the combination of the conservative hair spray inhalation exposure assessment parameters, in particular assuming an airspace volume of 2 m^3, and the aggregate exposure from use of the dermally applied products, which assumes a conservative 100% absorption rate, is sufficiently protective to cover additional inhalation exposure to the notified chemical from use of other spray cosmetic and household products with lower exposure factors (e.g. air fresheners).

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 > 2,000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	irritating
Rabbit, eye irritation	irritating
Mouse, skin sensitisation – local lymph node assay	no evidence of sensitisation
Rat, repeat dose toxicity - 28 days	NOAEL = 300 mg/kg bw/day
Mutagenicity - Induction of Point Mutations	non mutagenic
Genotoxicity – *in vitro* mammalian chromosome aberration	non genotoxic

Toxicokinetics, metabolism and distribution.
Based on the water solubility (0.461 g/L at 20 ºC), partition coefficient (log K_{ow} = 3.52) and the low molecular weight (< 500 Da) of the notified chemical, passive diffusion across the gastrointestinal (GI) tract and dermal absorption could occur. The notified chemical may also be absorbed across the respiratory tract.

Acute toxicity.
The notified chemical was found to have low acute oral and dermal toxicity in studies in rats.

No acute inhalation toxicity data were provided for the notified chemical.

Irritation.
In an acute dermal irritation study using three male New Zealand white rabbits, a single 4-hour, semi-occluded application of the notified chemical resulted in well-defined erythema and slight or moderate oedema and desquamation. The notified chemical is slightly irritating to the skin based on this study.

Two rabbit eye irritation studies on the notified substance were conducted by separate testing laboratories. In the first study only one rabbit was used and in the second study two rabbits were used and it was designed to complete the first study. Based on these studies the notified chemical is considered to be irritating to the eye.

Sensitisation.
The notified chemical at concentrations up to 50% in a mouse Local Lymph Node Assay showed no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation.

Repeated Dose Toxicity
A 28 day repeat dose study by oral gavage was conducted in rats with the notified chemical at dose levels of 30, 300 and 1000 mg/kg/day. Changes in liver weights and body weight gain along with histopathological findings in the high dose group were considered to be adverse and hence the lower dose of 300 mg/kg bw/day was chosen as the No Observed Adverse Effect Level (NOAEL) for systemic toxicity.

Mutagenicity/Genotoxicity.
The notified chemical was not mutagenic in a bacterial reverse mutation study (in the presence or absence of metabolic activation) and was not clastogenic in an in vitro mammalian chromosome aberration test.

Health hazard classification
Based on the available information, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard classification	*Hazard statement*
Eye Irritation (Category 2A)	H319 – Causes serious eye irritation

Based on the available information, the notified chemical is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), with the following risk phrase:
Xi: R36: Irritant to eyes

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Hairdressers, beauticians, cleaners and sales workers may be exposed to the notified chemical at ≤ 1% concentration when applying products containing it to clients. The risk for beauty care professionals who regularly use products containing the notified chemical is expected to be similar to that experienced by members of the public who use such products on a regular basis. For details of the public health risk assessment, see Section 6.3.2.

Workers involved in the reformulation of the imported products into cosmetic products may be exposed to the notified chemical at concentrations up to approximately 10%. Exposure is expected to be limited during product reformulation by the engineering controls and the PPE used.

Under the proposed occupational settings the notified chemical is not considered to pose an unreasonable risk to workers.

6.3.2. Public Health
The general public will be repeatedly exposed to the notified chemical during the use of both rinse-off and leave-on cosmetics, toiletries and household products containing the notified chemical at up to 1% concentration.

Local effects
From the dermal irritation study, the notified chemical did not meet the classification to be a skin irritant or corrosive. Skin irritation effects are not expected from use of the notified chemical at the concentrations in cosmetic and household products. However, the potential for eye irritation may be of concern, namely from use of hair spray and fine fragrances, which may be dispensed via a spray. Potential for ocular irritation from shampoo products should be mitigated by dilution with water and the rinse-off nature. This ocular exposure is only expected to occur in the unlikely event of an accident, and, in the case of household products, the products may be diluted with water at the time of eye contact. The potential for eye irritation is further reduced by the low proposed usage concentrations in the various products (≤ 1%).

Systemic effects
The potential systemic exposure to the public from the use of the notified chemical in cosmetic and household products was estimated to be 1.756 mg/kg bw/day. Using a NOAEL of 300 mg/kg bw/day, which was derived from a 28 day repeated dose toxicity study on the notified chemical, the margin of exposure (MOE) was estimated to be 171. A MOE value greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences, therefore, the MOE is considered to be acceptable.

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at ≤ 1% in fine fragrances and household products and at ≤ 0.5% cosmetics and toiletries is not considered to be unreasonable.

6. 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 are expected to 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% or up to 2 kg 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 is expected to be released to sewers in domestic situations across Australia as a result of its use in cosmetic and domestic products, which are either washed off the hair and skin of consumers, or disposed of following cleaning activities.

RELEASE OF CHEMICAL FROM DISPOSAL

It is estimated that a maximum of 3% of the consumer products 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 is expected to enter the sewer system before potential release to surface waters on a nationwide basis. The majority of the notified chemical will enter the sewer system as a result of the use of this chemical as component of fragrance preparations such as cosmetic and household care products. The notified chemical is not readily biodegradable and, based on its low adsorption coefficient (log Koc = 1.9-2.4), only limited partitioning to sludge is expected. The notified chemical is not likely to bioaccumulate based on its low bioconcentration factor. In surface waters, the notified chemical is expected to disperse and degrade through biotic and abiotic processes to form water and oxides of oxygen.

The half-life of the notified chemical in air is calculated to be 10 h based on reactions with hydroxyl radicals (AOPWIN v1.92, US EPA, 2009). Therefore, in the event of release to atmosphere, the notified chemical is not expected to persist in the atmospheric compartment.

A proportion of notified chemical may be applied to land when effluent is used for irrigation or when sewage sludge is used for soil remediation, or disposed of to landfill. Notified chemical residues in landfill, soil and sludge are expected to have medium to high mobility based on its high water solubility and its predicted soil adsorption coefficient (log K_{oc} = 1.9-2.4). Whilst not readily biodegradable, the notified chemical is not expected to persist in the terrestrial compartment and is expected to degrade to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

Since most of the notified chemical will be washed into the sewer, under a worst case scenario, with no removal of the notified polymer in the sewage treatment plant, the resultant Predicted Environmental Concentration (PEC) in sewage effluent on a nationwide basis is estimated as follows:

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

Dilution Factor - Ocean	10.0	
PEC - River:	0.61	µg/L
PEC - Oce□n:	0.06	µg/L

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 0.606 µg/L may potentially result in a soil concentration of approximately 4.039 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 20.19 µg/kg and 40.39 µg/kg, respectively.

7.2. Environmental Effects Assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Acute		
Daphnia Toxicity	48 h EC50 = 15 mg/L	Harmful to aquatic invertebrates
Algal Toxicity	72 h E_rC50 = 54 mg/L	Harmful to algae
Micro-organism	3h EC50 = 440 mg/L	Not expected to inhibit microbial respiration

Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) the notified chemical is harmful to aquatic invertebrates and is formally classified as 'Acute Category 3: Harmful to aquatic life. On the basis of the acute toxicity and the lack of ready biodegradability, the notified chemical is classified 'Chronic Category 3: Harmful to aquatic life with long lasting effects.

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) has been calculated from the acute Daphnia toxicity of the notified chemical and an assessment factor of 1000 as measured acute endpoints are available for two trophic levels.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LC50 (Daphnia).	15	mg/L
Assessment Factor	1000	
PNEC:	15	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:	0.61	15	0.04
Q - Ocean:	0.06	15	0.004

The risk quotient for discharge of treated effluents containing the notified chemical to the aquatic environment indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations based on its annual importation quantity. The notified chemical has a low potential for bioaccumulation and is unlikely to persist in surface waters, soil or air. Therefore, on the basis of the PEC/PNEC ratio, maximum annual importation volume and assessed use pattern in cosmetic and domestic products, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point 2 ± 0.5 °C

Method	OECD TG 102 Melting Point/Melting Range. EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature.
Remarks	Carried out in duplicate using a dry ice/isopropanol bath.
Test Facility	Firmenich (2002)

Boiling Point 208 ± 0.5 °C at 97.4 kPa

Method	EC Council Regulation No 440/2008 A.2 Boiling Temperature.
Remarks	Determined according to the Siwoloboff method.
Test Facility	Firmenich (2002)

Density 892 kg/m^3 at 20 ± 5 °C

Method	OECD TG 109 Density of Liquids and Solids. EC Council Regulation No 440/2008 A.3 Relative Density.
Remarks	Determined using the oscillating density meter method
Test Facility	Firmenich (2002)

Vapour Pressure 0.006 kPa at 20 °C
0.012 kPa at 25 °C

Method	OECD TG 104 Vapour Pressure. EC Directive 761/2009/EEC A.4 Vapour Pressure. OPPTS 830.7950 Vapour Pressure
Remarks	Determined using the isothermal thermogravimetric effusion method.
Test Facility	WIL (2013a)

Water Solubility 0.461 g/L at 20 °C

Method	EC Council Regulation No 440/2008 A.6 Water Solubility.
Remarks	Flask Method
Test Facility	Safepharm (2003a)

Partition Coefficient (n-octanol/water) log Pow = 3.52.at 20 °C

Method	EC Council Regulation No 440/2008 A.8 Partition Coefficient.
Remarks	HPLC Method
Test Facility	Safepharm (2003a)

Surface Tension 44.2 mN/m at 20 °C

Method	OECD TG 115 Surface Tension of Aqueous Solutions. EC Council Regulation No 440/2008 A.5 Surface Tension.
Remarks	Concentration: 90% of the test substance saturation solubility in water.
Test Facility	WIL (2013a)

Flash Point 90 ± 2 °C at 101.325 kPa

Method	EC Council Regulation No 440/2008 A.9 Flash Point.
Remarks	Determined using a closed cup equilibrium method.
Test Facility	Firmenich (2002)

Autoignition Temperature 260 °C

Method	EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases). DIN 51794
Remarks	No significant protocol deviations
Test Facility	WIL (2013a)

Explosive Properties Not expected to explosive

Method	The structure of the test material was assessed for chemical groups that imply explosive properties.
Remarks	The test substance contained no chemical groups that would imply explosive properties.
Facility	Firmenich (2013)

Oxidizing Properties Predicted negative

Method	The structure of the test material was assessed for chemical groups that imply oxidising properties.
Remarks	The test substance contained no chemical groups that would imply oxidising properties.
Facility	Firmenich (2013)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain	Rat/Sprague Dawley CD
Vehicle	Test substance administered as supplied
Remarks - Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3 F	2,000	0/3
2	3 F	2,000	0/3

LD50	> 2,000 mg/kg bw
Signs of Toxicity	There were no unscheduled deaths during the study. Clinical signs that were observed in the treated animals included hunched posture, lethargy, ataxia, decreased respiratory rate and laboured respiration.
Effects in Organs	No adverse macroscopic findings were recorded at necroscopy. One animal was noted in necropsy findings to have hydronephrosis (congenital condition, found in the left kidney), which was not considered to be test- material related.
Remarks - Results	All animals showed the expected gains in bodyweight over the study period.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Safepharm (2002a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 402 Acute Dermal Toxicity. EC Council Regulation No 440/2008 B.3 Acute Toxicity (Dermal).
Species/Strain	Rat/Wistar
Vehicle	Test substance administered as supplied
Type of dressing	Occlusive
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	5 per sex	2,000	1/10

LD50	> 2,000 mg/kg bw
Signs of Toxicity -Local	Swelling, fissures, general or maculate erythema, scales/scabs were seen on the treated skin areas.
Signs of Toxicity - Systemic	The single mortality occurred on day 2 after treatment in a male rat. Hunched posture, lethargy, uncoordinated movements, piloerection, hypothermia, chromodacryorrhoea and/or ptosis were observed with symptoms resolving between days 2 and 4 after treatment.
Effects in Organs	Macroscopic examination of the male rat that died on day 2 after treatment revealed dark red discolouration of the mandibular lymph nodes. Macroscopic post mortem examination of the surviving animals

did not reveal any abnormalities.

Remarks - Results: The increases in body weights of the test animals over the test period fell in the expected range and were therefore considered not indicative of toxicity.

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

TEST FACILITY: WIL Research (2013b)

B.3. Irritation – skin

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 404 Acute Dermal Irritation/Corrosion.
EC Council Regulation No 440/2008 B.4 Acute Toxicity (Skin Irritation).
Directive 92/69/EEC Method B4 Acute Toxicity (Skin Irritation)

Species/Strain: Rabbit/New Zealand White
Number of Animals: 3 Male
Vehicle: Test substance administered as supplied
Observation Period: 14 days
Type of Dressing: Semi-Occlusive (Cotton gauze covered by elasticated corset)
Remarks - Method: No significant protocol deviations.
A single 4 hour application of the test material was made to the intact skin of 3 male rabbits. Test sites were observed for evidence of primary irritation at 1, 24, 48 and 72 hours post patch removal.

RESULTS

Skin Reaction	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	1	2	1.7	2	≤ 7 days	0
Oedema	0.7	1.7	1	2	≤ 7 days	0

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

Remarks - Results: Well defined erythema was noted for 2 of the test animals at the 24 and 48 hour observations with very slight erythema in the remaining animal. One test animal continued to display well defined erythema at the 72 hour observation, with the other test animals' reactions subsiding to very slight erythema. Very slight to slight oedema was noted at the treated skin areas of all the test animals. All treated skin sites appeared normal at the day 14 observation.

CONCLUSION: The notified chemical is slightly irritating to the skin.

TEST FACILITY: Safepharm (2002b)

B.4. Irritation – eye

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 405 Acute Eye Irritation/Corrosion.
EC Council Regulation No 440/2008 B.5 Acute Toxicity (Eye Irritation).

Species/Strain: Rabbit/New Zealand White
Number of Animals: 1 Male and 1 Female
Observation Period: 12 days
Remarks - Method: No significant protocol deviations.
This study was designed to be a completion of the early study below which only used one test animal.

RESULTS

Lesion	*Mean Score* Animal No.*		*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2			
Conjunctiva: redness	3.0	2.3	3	< 12 days	0
Conjunctiva: chemosis	3.3	2.0	4	< 12 days	0
Conjunctiva: discharge	**	**	**	< 7 days	0
Corneal opacity	3.0	2.0	4	< 11 days	0
Iridial inflammation	†	0.3	0	< 7 days	0

* Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.
** Whitish purulent discharge was observed but not scored
† Scoring masked by the corneal opacity

Remarks - Results: A single application of 0.1 mL of the test material to the non-irrigated eye of two rabbits produced moderate conjunctival irritation, slight iritis and severe corneal opacity. All treated eyes appeared normal at the day 12 observation.

CONCLUSION: The notified chemical is irritating to the eye.

TEST FACILITY: CIT (2004)

B.5. Irritation – eye

TEST SUBSTANCE: Notified chemical

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

Species/Strain: Rabbit/New Zealand White
Number of Animals: 1 Male
Observation Period: 7 days
Remarks - Method: No significant protocol deviations.

RESULTS

Lesion	*Mean Score* For test animal*	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1			
Conjunctiva: redness	2	3	< 7 days	0
Conjunctiva: chemosis	1.67	2	< 7 days	0
Conjunctiva: discharge	1.67	3	< 7 days	0
Corneal opacity	1.67	2	< 7 days	0
Iridial inflammation	0.67	1	< 72 hours	0

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

Remarks - Results: A single application of 0.1 mL of the test material to the non-irrigated eye of one rabbit produced translucent corneal opacity, iridial inflammation and severe conjunctival irritation. Dulling of the normal lustre of the cornea was also noted at the 1 hour observation. The treated eye appeared normal at the 7 day observation.

CONCLUSION: The notified chemical is irritating to the eye.

TEST FACILITY: Safepharm (2002c)

B.6. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 429 Skin Sensitisation: Local Lymph Node Assay EC Directive 2004/73/EC B.42 Skin Sensitisation (Local Lymph Node Assay)
Species/Strain	Mouse/CBA/Ca (CBA/CaCruBR)
Vehicle	Acetone/olive oil (4:1 v/v)
Remarks - Method	No significant protocol deviations. Topical application was made to the dorsal surface of the ear. A concurrent positive control study was not run, but previously conducted positive control data from the test laboratory was provided.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	1235.908 (± 153.70)	
0.5	824.25 (± 295.74)	0.67
5	1434.106 (± 417.56)	1.16
50	1911.736 (± 292.75)	1.55

Remarks - Results	No mortalities and no signs of systemic toxicity were noted in the test or control animals. The results show that the test substance elicited stimulation indices <3. A statistically significant difference ($p < 0.01$) was noted between the control group and the 50% dose group. The positive controls gave satisfactory responses confirming the validity of the test system.
CONCLUSION	There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.
TEST FACILITY	Safepharm (2002d)

B.7. 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™:RccHan™:WIST
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week
Vehicle	Arachis Oil
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5 per sex	0	0/0
low dose	5 per sex	30	0/0
mid dose	5 per sex	300	0/0
high dose	5 per sex	1,000	0/0

Mortality and Time to Death

There were no unscheduled deaths during the study.

Clinical Observations

Analysis of clinical appearance, functional observations, and food and water consumption did not reveal any toxicologically significant abnormalities between the treated and the control groups. Clinical signs that some test animals exhibited above 300 mg/kg bw/day, such as increased salivation and staining around the mouth, were dismissed by the study authors as commonly observed following the oral administration of unpalatable or slightly irritant test material formulations and in isolation were not considered to be of toxicological importance.

Male animals in the 300 and 1,000 mg/kg bw/day treatment groups showed statistically significant reductions in body weight gain in weeks 3 and 4 respectively. No effects were observed in females at any dose or male animals at a dose of 30 mg/kg bw/day. There were no statistically significant differences in the mean bodyweights of the different groups.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Female test animals from all treatment groups showed statistically significant increases in lymphocyte and total leucocyte count. Females treated with 1000 mg/kg bw/day also showed statistically significant increase in neutrophil count and reduction in activated partial thromboplastin time. Males from all treatment groups showed a statistically significant reduction in clotting time. All individual values were within the normal ranges for rats of the strain and age used and lacked a discernible dose response relationship, therefore the intergroup differences were considered not to be of toxicological importance.

There were noted increases in creatinine in both sexes and female test animals displayed significant decreases in glucose and urea. Again all individual values were within the normal ranges for rats of the strain and age used and in the absence of any associated histology correlates at this level, the intergroup differences were considered by the study authors not to be of toxicological importance.

Effects in Organs

Statistically significant higher absolute (14%) and relative liver weight was noted in females treated at 1000 mg/kg bw/day. Males treated at ≥ 300 mg/kg bw/day exhibited statistically significant reduction in absolute liver weight (3.2% and 1.1% for the 300 and 1,000 mg/kg bw/day treatment groups respectively), but an increase in relative liver weight. No toxicologically significant effects were detected in both sexes in the test animals treated below those doses.

Females treated with doses 300 mg/kg bw/day and over showed a statistically significant increase in uterus/cervix and a decrease in heart weight both absolute and relative to terminal body weight. Males treated with 30 mg/kg bw/day showed a statistically significant reduction in absolute and relative spleen weight. In the absence of any histopathology correlates or a true dose related response, the study authors considered these intergroup differences not to be of toxicological importance.

Males treated with 1000 mg/kg bw/day showed a statistically significant reduction in epididymis weight. The histolopathological examinations of two males from this high dose group showed aspermia. The study authors considered these findings to possibly be a consequence of stress induced change or an incidental finding since such events may also occur in the control group males. The remaining high dose males showed epididymis weights in the normal range, therefore this intergroup difference was considered not to be of toxicological significance.

Other notable histopathological findings were seen in the high dose groups for both sexes. Minimal centrilobular hepatocellular hypertrophy was evident in all 1000 mg/kg bw/day animals. Slight diffuse follicular cell hypertrophy in the thyroid gland was noted in a few animals of both sexes treated with 1000 mg/kg bw/day. Slight basophilic cell hypertrophy in the pituitary gland was seen in a few animals of both sexes of the high dose group, seen as groups of cells in the males but only single cells in one affected female. These changes were not considered by the study authors to be adverse and/or of toxicological relevance.

Minimally increased severity of tubular basophilia and hyaline droplet formation were present in high dose group males. The kidney effects of males in the high dose test group were considered to represent an adverse effect of the test item. The study authors claim these kidney changes of hyaline droplets were consistent with well documented changes that are peculiar to the male rat in response to treatment with some hydrocarbons. The

study authors also attributed this peculiarity to the other kidney effects of tubular basophilia and degeneration. They hence found these effects not indicative of a hazard to human health.

Remarks – Results
The changes in liver weights and body weight gain along with histopathological findings in the high dose group were considered to be adverse and hence the lower dose of 300 mg/kg bw/day was the dose where no adverse treatment related effects were observed.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) for systemic toxicity was established by the study authors as 300 mg/kg bw/day based on adverse effects at the highest dose tested.

TEST FACILITY Harlan (2012)

B.8. 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.
Ames test- Plate incorporation procedure

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA102, TA98 and TA100
Metabolic Activation System	S9 fraction from phenobarbitone/β-naphthoflavone induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 5 – 5,000 µg/plate b) Without metabolic activation: 5 – 5,000 µg/plate
Vehicle	Dimethyl sulfoxide
Remarks - Method	A range finding test was conducted using TA100 and WP2uvrA with and without metabolic activation between 0.15 – 5000 µg/plate.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 1,500	≥ 1,500	> 5,000	negative
Test 2		≥ 1,500	> 5,000	negative
Present				
Test 1	≥ 1,500	≥ 1,500	> 5,000	negative
Test 2		≥ 1,500	> 5,000	negative

Remarks - Results
No test material precipitate was observed at any of the doses tested in either the presence or absence of S9-mix.

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

The positive controls produced satisfactory responses, thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.

The test substance caused a visible reduction in the growth of the bacterial background lawn, with and without metabolic activation.

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

TEST FACILITY Safepharm (2002e)

B.9. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 473 In vitro Mammalian Chromosome Aberration Test. EC No. 440/2008 B.10 Mutagenicity – In Vitro
Species/Strain	Human
Cell Type/Cell Line	Lymphocytes
Metabolic Activation System	S9 fraction from phenobarbital/β-naphthoflavone induced rat liver
Vehicle	Dimethyl sulfoxide
Remarks - Method	A preliminary cytogenetic assay were performed: tested both with and without the metabolic activation system (at 1.8% v/v) for concentrations up to 333 µg/mL with 3 hour exposure time and 24 hour fixation time. Precipitation was noted in the culture medium at this dose level. Cell lysis were noted at ≥ 1000 µg/mL. Vehicle and positive controls (mitomycin C without metabolic activation and cyclophosphamide with metabolic activation) were used in parallel with the test substance.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 3, 10, 33*, 100*, 333*	3 h	24 h
Test 2a	0*, 3*, 30, 100*, 150*, 200, 250, 300	24 h	24 h
Test 2b	0*, 3*, 30, 50, 70, 90, 100*, 200*	48 h	48 h
Present			
Test 1	0*, 3, 10, 33*, 100*, 333*	3 h	24 h
Test 2	0*, 30*, 100*, 333*	3 h	48 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	≥ 100	> 333	≥ 333	negative
Test 2a		≥ 150	≥ 200	negative
Test 2b		≥ 200	≥ 200	negative
Present				
Test 1	> 333	> 333	≥ 333	negative
Test 2		> 333	≥ 333	negative

Remarks - Results	There were no toxicologically (or statistically) significant increases in the number of cells with aberrations, with or without metabolic activation. The study authors also note that there were no effects on the number of polyploid cells and cells with endoreduplicated chromosomes, with or without metabolic activation. The study authors claim the test material does not disturb mitotic processes and cell cycle progression. The positive and vehicle controls gave satisfactory responses confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic to human lymphocytes treated in vitro under the conditions of the test.
TEST FACILITY	WIL Research (2013c)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test.
Inoculum	Activated sewage sludge from a predominantly domestic sewage treatment plant
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Dissolved Oxygen Method (DOC) Method
Remarks - Method	Conducted in accordance with the test guidelines above, and in compliance with GLP standards and principles.

RESULTS

Notified chemical		*Sodium benzoate (reference substance)*		*Notified chemical and sodium benzoate (inhibition check)*	
Day	*% Degradation*	*Day*	*% Degradation*	*Day*	*% Degradation*
3	1	3	53	3	22
15	9	15	77	14	28
28	11	28	78	28	31

Remarks - Results

The oxygen depletion of the inoculated control did not exceed 1.5 mg O_2/L after 28 days. The residual oxygen concentration in the test bottles remained at 3.8 mg O_2/L or greater in all test vessels therby satisfying the validity criteria.

Examination of the degradation curve for the toxicity control showed that the toxicity control attained in excess of 25% degradation by day 14 of the study thereby confirming that the notified chemical was not toxic to the sewage treatment micro-organisms used in the study. After 28 days the toxicity control had attained 31% degradation.

The notified chemical attained 11% degradation after 28 days and, therefore, cannot be considered as readily biodegradable under the conditions of OECD Guideline 301D.

CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	Safepharm (2003b)

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 and Reproduction Test - Static. EC Council Regulation No 440/2008 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	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. No significant deviations to the test protocol were reported. As the test substance was suspected to be a volatile substance, the test was performed in a closed system The test was performed at 20 ºC; pH 7.9-8.0.

RESULTS

Nominal Concentration mg/L	*Measured Concentraions mg/L*	*Number of D. magna*	*Number Immobilised*	
			24 h	*48 h*
Control	-	10	0	0
1.0	1.62	10	0	0
1.8	-	10	0	0
3.2	2.98	10	0	0
5.6	-	10	0	0
10	10.1	10	0	0
18	-	10	0	17
32	31	10	2	20
56	-	10	5	20
100	95.2	10	20	20

LC50	15 mg/L at 48 hours (95% confidence limit: 13-16 mg/L).
NOEC	10 mg/L at 48 hours
Remarks - Results	The validity criteria for the test were met. After 48 hours, no immobilisation was observed up to a test concentration of 10 mg/L while 100% immobilisation occurred at 32 mg/L and above Due to the steepness of the concentration-effect relationship the EC50 could not be calculated using typical statistical analysis such as probit analysis. Instead, the trimmed Spearman-Karber method (Hamilton et al 1977) at 48 hours based on the nominal test concentrations. Analysis of the test preparations at 0 and 48 hours showed measured test concentrations to range from 92% to 102% of nominal value with the exception of the 1.0 mg/l test concentration at 0 and 48 hours which showed measured test concentrations of 162% and 181% of nominal value respectively. These high measured concentrations were considered to be due to an undefined reason. However, as this concentration was below the No Observed Effect Concentration of 10 mg/l it was considered justifiable to calculate the EC50 values in terms of the nominal test concentrations only.
CONCLUSION	The notified chemical is harmful to aquatic invertebrates
TEST FACILITY	Safepharm (2004)

C.2.2. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test. EC Council Regulation No 440/2008 C.3 Algal Inhibition Test - Static.
Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: 1.0, 3.2, 10, 32 and 100 mg/L. Actual: 0.63, 2.0, 6.7, 26, 74 and 85 mg/L (time weighted average).

Auxiliary Solvent	None
Water Hardness	24 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. No significant deviations to the test protocol were reported. Test conditions: 21-24 ºC; pH 8.1 ±-0.2.

RESULTS

Biomass		*Growth*	
E_yC50 mg/L at 72 h	*NOEC mg/L*	*E_rC50 mg/L at 72 h*	*NOEC mg/L*
19 (95% confidence limits: 8.6-43)	6.7	54.0 (based on time weighted average) (95% confidence limits: 12-240)	6.7

Remarks - Results	The validity criteria for the test were met. The tests were performed on a standard manner despite the indication that the test substance is volatile. The concentrations present during the test caused significant effects which allowed determination of the EC50 values for growth rate and yield, based on time weighted average concentrations.
CONCLUSION	The notified chemical is harmful to algae
TEST FACILITY	WIL Research (2013d).

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	Activated sewage sludge from domestic sewage treatment plant
Exposure Period	3 hours
Concentration Range	Nominal loading: 46, 100, 220, 460 and 1000 mg/L Actual: Not measured
Remarks – Method	The test was conducted in accordance with the test guideline without significant deviations. Good Laboratory Practice (GLP) was followed.
RESULTS	
EC50	440 mg/L at 3 hours (95% CI 340-560 mg/L)
NOEC	220 mg/L
Remarks – Results	All validity criteria were satisfied and no significant deviations to protocol were reported.
CONCLUSION	The notified chemical is not expected to be inhibitory to micro-organisms at concentrations < 440 mg/L.
TEST FACILITY	WIL Research (2013e).

BIBLIOGRAPHY

Cadby, PA, Troy, WR and Vey, MGH (2002) Consumer Exposure to Fragrance Ingredients: Providing Estimates for Safety Evaluation. Regulatory Toxicology and Pharmacology, 36: 246-252.

CIT (2004) ST 44 C 01: Acute Eye Irritation in Rabbits (Study No. 26711 TAL, March, 2004). Evreux, France, Safety & Health Research Laboratories (Unpublished report submitted by the notifier).

Firmenich SA (2002) Determination of General Physico-Chemical Properties: ST 44 C 01 (Study No. R006-08.2002, September, 2002). Meyrin, Switzerland, Firmenich Laboratory of Analysis and Measurements La Plaine (Unpublished report submitted by the notifier).

Firmenich SA (2013) Statement: Oxidising, explosive and flammability properties of Firanol (August, 2013). Meyrin, Switzerland, Firmenich Laboratory of Analysis and Measurements La Plaine (Unpublished report submitted by the notifier).

Harlan (2012) ST 19 C 11: Twenty-Eight day Repeated Dose Oral (Gavage) Toxicity Study in the Rat (Project No. 41102670, March, 2012). Derbyshire, United Kingdom, Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

NOHSC (2004) Approved Criteria for Classifying Hazardous Substances, 3rd edition [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

NTC (National Transport Commission) 2007 Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), 7th Edition, Commonwealth of Australia.

Safepharm (2002a) ST 44 C 01: Acute Oral Toxicity in the Rat- Acute Toxic Class Method (Study No. 161/360, November, 2002). Derbyshire, United Kingdom, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (2002b) ST 44 C 01: Acute Dermal Irritation in the Rabbit (Study No. 161/361, December, 2002). Derbyshire, United Kingdom, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (2002c) ST 44 C 01: Acute Eye Irritation in the Rabbit (Study No. 161/362, December, 2002). Derbyshire, United Kingdom, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (2002d) ST 44 C 01: The Local Lymph Node Assay in the Mouse (Study No. 161/354, December, 2002). Derby, United Kingdom, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (2002e) ST 44 C 01: Reverse Mutation Assay “Ames Test” using *Salmonella Typhimurium* (Study No. 161/350, July, 2002). Derby, United Kingdom, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (2003a) ST 44 C 01: Determination of General Physico-Chemical Properties (Study No. 161/358, January, 2003). Derbyshire, United Kingdom, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (2003b) ST 44 C 01: Assessment of Ready Biodegradability; Closed Bottle Test (Study No. 161/363, March, 2003). Derbyshire, United Kingdom, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (2004) ST 44 C 01: Acute Toxicity to *Daphnia magna* (Study No. 161/425, April, 2004). Derbyshire, United Kingdom, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

SCCS (2012) Notes of Guidance for testing of Cosmetic Ingredients and Their Safety Evaluation (8th revision). European Commission - Scientific Committee on Consumer Safety.

SWA (2012) Code of Practice: Managing Risks of Hazardous Chemicals in the Workplace, Safe Work Australia, http://www.safeworkaustralia.gov.au/sites/swa/about/publications/pages/managing-risks-of-hazardous-chemicals-in-the-workplace.

United Nations (2009) Globally Harmonised System of Classification and Labelling of Chemicals (GHS), 3rd revised edition. United Nations Economic Commission for Europe (UN/ECE), <http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html >.

US EPA (2009) Estimations Programs Interface Suite™ for Microsoft® Windows, v 4.00. United States Environmental Protection Agency. Washington, DC, USA. Accessed on 15 January 2014.

WIL Research (2013a) Determination of Physico-Chemical Properties of ST 20 C 12 (Project No. 501617, May, 2013). S'-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL Research (2013b) Assessment of Acute Dermal Toxicity with ST 20 C 12 in the Rat (Project No. 501619, April, 2013). S'-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL Research (2013c) Evaluation of the ability of ST 20 C 12 to induce Chromosome Aberrations in cultured Peripheral Human Lymphocytes (with repeat experiment) (Project No. 501620, April, 2013). S'-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL Research (2013d) Fresh Water Algal Growth Inhibition with ST 20 C 12 (Project No. 501621, September, 2013). S'-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL Research (2013e) Activated Sludge Respiration Inhibition Test (Carbon and Ammonium Oxidation) with ST 20 C 12 (Project No. 501622, April, 2013). S'-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).