File No: LTD/1564

March 2012

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Centifolether

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 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:

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

Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS SUBSTANCE	INTRODUCTION VOLUME	USE
LTD/1564	Firmenich Limited	Centifolether	Yes	<1 tonne per annum	Component of cosmetic and household cleaning products

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the data provided, the notified chemical is not classified 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, 2009) is presented below. The environmental classification under this system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	***Hazard statement***
Aquatic Environment	Acute Category 2	Toxic to aquatic life

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 PEC/PNEC ratio, maximum annual importation volume and assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations
CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following isolation and engineering controls to minimise occupational exposure to the notified chemical during reformulation processes:
  - Enclosed, automated processes, where possible

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical during reformulation processes:
  - Avoid contact with skin and eyes

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical during reformulation processes:
  - Coveralls, impervious gloves, goggles

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

- 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.

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;
  - the concentration of the chemical exceeds or is intended to exceed 1.15% in fine fragrances, 2.5% in other cosmetic products and 5% in household cleaning products.

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of cosmetic and household cleaning products, 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.

ASSESSMENT DETAILS

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

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, degree of purity, impurities and additives/adjuvants,.

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

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
Low Volume Chemical (LVC) permit

NOTIFICATION IN OTHER COUNTRIES
USA (1999), Philippines (2000), EU (1999), Switzerland (1999),

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Centifolether

MOLECULAR WEIGHT
<500 Da

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

3. COMPOSITION

DEGREE OF PURITY >90%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 ºC AND 101.3 kPa: colourless liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	<-50ºC	Measured
Boiling Point	219.4 ± 0.4 ºC at 100.28 kPa	Measured
Density	0.925 kg/m^3 at 20ºC	Measured
Vapour Pressure	0.0343 kPa at 25 ºC	Measured
Water Solubility	0.270 g/L	Measured
Hydrolysis as a Function of pH	≤20% after 28 days (40 ºC, pH 5-12) ≤30% after 28 days (40 ºC, pH 2)	Measured
Partition Coefficient	Log Pow = 3.38	Measured

(n-octanol/water)		
Adsorption/Desorption	Log Koc = 2.7	Calculated (KOCWIN v2.00, from log Kow, US EPA, 2009). Expected to have medium to low mobility in soil.
Dissociation Constant	Not determined	Contains no dissociable functionality
Flash Point	84 ºC at 101.1 kPa	Measured
Flammability	Not flammable in contact with water	Measured
Autoignition Temperature	390 ± 5 ºC	Measured
Explosive Properties	Predicted negative	Contains no functional groups that would imply explosive properties.
Oxidising Properties	Predicted negative	Contains no functional groups that would imply oxidative properties.

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties not assessed by the US EPA, refer to Appendix A.

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

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 be imported into Australia as a component (≤5%) 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

IDENTITY OF MANUFACTURER/RECIPIENTS
Firmenich Ltd

TRANSPORTATION AND PACKAGING
The fragrance preparations containing the notified chemical (at ≤5% concentration) will be imported in tightly closed lacquered drums, typically of 180 kg size, but also 100, 50, 25, 10 or 5 kg. They will be transported by road from the wharf or airport of entry to the Firmenich Ltd warehouse for storage and then distributed to reformulation sites. The end-use products will be packaged in containers suitable for retail sale.

USE
The notified chemical is intended to be used as a component of fragrances for a variety of cosmetic and household cleaning products (proposed usage concentration: ≤1.15% concentration in fine fragrances, ≤2.5% in other cosmetic products and ≤5% in household cleaning products).

OPERATION DESCRIPTION
The procedures for incorporating the imported preparations (containing ≤5% notified chemical) into end-use products will likely vary depending on the nature of the cosmetic and personal care/household cleaning products 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 a fully enclosed environment, followed by automated filling of the reformulated end-use products into containers of various sizes.

The end-use products containing the notified chemical may be used by consumers and professionals such as hairdressers, workers in beauty salons 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.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport workers	Unknown	Unknown
Mixer	4	2
Drum Handling	4	2
Drum Cleaning	4	2
Maintenance	4	2
Quality Control	0.5	1
Packaging	4	2
Salon Workers	Unspecified	Unspecified
Cleaners	Unspecified	Unspecified

EXPOSURE DETAILS
Transport and storage workers may come into contact with the notified chemical, as a component of the imported preparations or end-use products (≤5%) only in the event of accidental rupture of containers.

During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified chemical (at ≤5% concentration) may occur during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. Exposure is expected to be minimised through the use of mechanical ventilation and/or enclosed systems and through the use of personal protective equipment such as coveralls, safety glasses and impervious gloves.

Exposure to the notified chemical in end-use products (at ≤5% concentration) may occur in professions where the services provided involve the application of cosmetic and personal care products to clients (e.g. hairdressers, workers in beauty salons) or in the cleaning industry. Such professionals may use some personal protective equipment to minimise repeated exposure, and 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 widespread and repeated exposure of the public to the notified chemical (at ≤5% concentration) through the use of the household cleaning products and the 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.

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
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics, metabolism and distribution.
Based on the water solubility (0.270 g/L), partition coefficient (log P_{ow} = 3.38) and the low molecular weight (<500 Da) of the notified chemical, passive diffusion across the gastrointestinal (GI) tract and dermal absorption are expected to occur. The notified chemical may also be absorbed across the respiratory tract.

Acute toxicity.
The notified chemical was found to be of low acute oral toxicity in rats. Acute dermal and inhalation toxicity data were not provided for the notified chemical.

Irritation and Sensitisation.
In a skin irritation study in rabbits, very slight to well-defined erythema and very slight to slight oedema were noted, with effects resolved within 9 days. In an eye irritation study in rabbits, mild to moderate conjunctival irritation was noted, with treated eyes appearing normal after 11 days. The irritation scores in these studies did not warrant classification of the chemical as a skin or eye irritant.

The notified chemical was not a skin sensitiser in guinea pigs (Magnusson-Kligman method).

Repeated Dose Toxicity (sub acute, sub chronic, chronic).
No repeated dose toxicity data were provided for the notified chemical.

Mutagenicity.
The notified chemical was not mutagenic in a bacterial reverse mutation study.

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

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Reformulation
Exposure of workers to the notified chemical (at ≤5% concentration) may occur during blending operations. While the notified chemical was found to be slightly irritating to the eyes and skin, irritant effects are not expected at the proposed introduction and usage concentrations. In addition, measures to minimise exposure including the use of appropriate PPE are expected to be in place. Therefore, the risk to the health of workers from use of the notified chemical is not considered to be unreasonable.

End-use
Cleaners and beauty care professionals will handle the notified chemical at ≤5% concentration, similar to public use. Therefore, the risk to workers who regularly use the notified chemical is expected to be of a similar or lesser extent than that experienced by members of the general public who use such products on a regular basis. For details of the public health risk assessment see section 6.3.2.

Based on the information available, the risk to workers associated with the use of the notified chemical at ≤1.15% concentration in fine fragrances, ≤2.5% in other cosmetic products and ≤5% in household cleaning products, is not considered to be unreasonable.

6.3.2. Public Health
At the proposed usage concentration of ≤1.15% notified chemical in fine fragrances, ≤2.5% in other cosmetic products and ≤5% in household cleaning products, acute toxicity effects are not expected. The repeated dose toxicity effects of the notified chemical have not been determined. However exposure is expected to be limited by the low concentration of the notified chemical in end-use products.

Therefore, the risk associated with use of the notified chemical at ≤1.15% concentration in fine fragrances, ≤2.5% in other cosmetic products and ≤5% in household cleaning products, is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will 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% 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 household cleaning 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 are likely to be disposed of through domestic garbage disposal and 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. An estimated 50% of the notified chemical is predicted to removed during sewage treatment plant (STP) processes (SimpleTreat; European Commission, 2003), with 37% removal by degradation, 9% by volatilisation and a further 4% removed through partitioning to sludge, before discharge to surface waters on a nationwide basis. The notified chemical is expected to be hydrolytically stable under the environmental conditions based on the provided studies and structural considerations. The notified chemical is not readily biodegradable (30% biodegradation in 21 days via the closed bottle test, OECD TG 301D, US EPA assessment, measured) but is considered to have potential for inherent biodegradability. The notified chemical is not likely to bioaccumulate based on its partition coefficient (log Pow = 3.38) and low predicted bioconcentration factor (log BCF = 1.9, US EPA assessment). In surface waters, the notified chemical is expected to disperse and degrade to form water and oxides of carbon.

The notified chemical is moderately volatile (log H = 1.316 Pa/m^3/mol, SimpleTreat, European Commission, 2003) and may volatilise to air during use or STP treatment. The half-life of the notified chemical in air is calculated to be ≤5.7 h based on reactions with hydroxyl radicals (US EPA assessment, predicted). 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 treated sewage effluent is used for irrigation or when sewage sludge is used for soil remediation, or disposed of to landfill. Despite having moderate water solubility, notified chemical residues in landfill, soil and sludge are expected to have low to medium mobility in soil based on its predicted soil adsorption coefficient (log Koc = 2.7), and are expected to degrade to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The following Predicted Environmental Concentrations (PEC) have been calculated assuming that all of the imported quantity of notified chemical will be released to sewer. Of this, an estimated 50% is predicted to be removed during sewage treatment plant (STP) processes (SimpleTreat, European Commission, 2003) before discharge to surface waters on a nationwide basis.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year

Daily chemical release:	2.74	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	50%	
Daily effluent production:	4,523	ML
Dilution Factor - River	1	
Dilution Factor - Ocean	10	
PEC - River:	0.30	µg/L
PEC - Ocean:	0.03	µg/L

Partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 0.242 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 0.002 mg/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 0.01 mg/kg and 0.02 mg/kg, respectively.

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 0.303 µg/L may potentially result in a soil concentration of approximately 2.019 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 10.10 µg/kg and 20.19 µg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity data were submitted. Estimated effects endpoints for aquatic organisms were calculated and are included in the table below.

Endpoint	*Result*	*Assessment Conclusion*
Acute Toxicity		
Fish Toxicity	96 h LC50 = 11.7 mg/L[1]	Harmful to fish
Daphnia Toxicity	48 h LC50 = 7.86 mg/L[1]	Toxic to aquatic invertebrates
Algal Toxicity	96 h EC50 = 6.22 mg/L[1]	Toxic to algae
Chronic Toxicity		
Fish Toxicity	30 d ChV = 1.32 mg/L[1]	Not harmful to fish with long lasting effects
Daphnia Toxicity	ChV = 1.10 mg/L[1]	Not harmful toxic to aquatic invertebrates with long lasting effects
Algal Toxicity	ChV = 2.89 mg/L[1]	Not harmful to algae with long lasting effects

[1] Modelled estimates (ECOSAR v1.00, class – neutral organics, KOWWIN calculated log Kow = 3.17, US EPA, 2009).

Based on the estimated endpoints in the absence of experimental data, under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) the notified chemical is harmful to fish and toxic to aquatic invertebrates and algae, and is formally classified as 'Acute Category 2: Toxic to aquatic life'.

The GHS classification for long-term hazard are based on NOEC (or equivalent EC*x*) endpoints, whereas the available endpoints are chronic values [ChV = (LOEC × NOEC)^{½}] which, by definition, are greater than the NOEC. On the basis of its lack of rapid degradability and the estimated ChV endpoints the notified chemical is, at best, not harmful with long lasting effects to fish, aquatic invertebrates and algae. Therefore, based on the estimated endpoints in the absence of experimental data, the notified chemical is formally not classified for long-term hazard under the GHS.

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) has been calculated from the estimated daphnid chronic 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 estimated chronic endpoints (ChV = (LOEC × NOEC)^{½}) for three trophic levels are available, these chronic endpoints are not no-observed effect concentrations (NOECs).

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
ChV (Invertebrates).	1.1	mg/L
Assessment Factor	50	
PNEC:	22	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:	0.30	22	0.014
Q - Ocean:	0.□3	22	0.001

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 and the partial removal of the chemical from waste water by degradation, volatilisation and sorption to sewage sludge. The notified chemical has a low potential for bioaccumulation and is unlikely to persist in surface waters, soil or the air. Therefore, on the basis of the PEC/PNEC ratio, maximum annual importation volume and assessed use pattern in cosmetic and household cleaning products, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Vapour Pressure 0.0343 kPa at 25 ºC

Method An internal non-GLP method
Remarks Dynamic Measurement.
Test Facility Firmenich (2010)

Hydrolysis as a Function of pH ≤20% after 28 days (40 ºC, pH 5-12)
≤30% after 28 days (40 ºC, pH 2)

Method In-house

pH	*T (ºC)*	*% hydrolysis after 28 days**
2	40	≤30
5	40	≤20
7	40	≤20
8.5	40	≤20
12	40	≤20

* Data points are approximated based on the provided graph

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, 4, 8, 15, 23 and 28.

Hydrolysis was less than 20% after 28 days storage at 40 ºC over pH 5-12 and less than 30% at pH 2. Based on the results the hydrolysis half life is expected to be greater than 2 months under environmental conditions (pH 4-9, 25 ºC). On the basis of structure, the notified chemical is expected to be hydrolytically stable under environmental conditions.
Test Facility Firmenich (2011a)

Flash Point 84 ºC at 100.1 kPa

Method EC Directive 92/69/EEC A.9 Flash Point.
Remarks Determined using Pensky-Martens closed cup flash point apparatus.
Test Facility Ineris (1998)

Flammability Not flammable in contact with water

Method EC Directive 92/69/EEC A.12 Flammability (contact with water)
Remarks In Contact with water, the test substance did not spontaneously ignite or give off flammable gas in excess of 1L/kg/h.
Test Facility Ineris (1998)

Autoignition Temperature 390 ± 5ºC at 98.1 kPa

Method Internal non-GLP method
Remarks Aliquots of the test substance were injected into a flask (in a flask heater) and the flask observed for any signs of ignition over a 300 second period. This process was repeated until ignition was repeated until ignition was observed within 300 seconds of insertion.
Test Facility Firmenich (2011b)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 401 Acute Oral Toxicity – Limit Test.
Species/Strain	Rat/Sprague Dawley OFA, 5M/5F
Vehicle	Carboxymethylcellulose
Remarks - Method	No significant protocol deviations
RESULTS	
Remarks - Results	There were no mortalities observed
LD50	>2,000 mg/kg bw
Signs of Toxicity	None
Effects in Organs	None
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Evic-Ceba, (1997a)

B.2. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand Albino
Number of Animals	3
Vehicle	None
Observation Period	14 days
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	1.7	2	0.7	2	<9 days	0
Oedema	0.3	0.7	0	2	<72 hours	0

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

Remarks - Results	Very slight to well-defined erythema and very slight to slight oedema were noted at up to the day 8 and day 2 observation, respectively. The effects were resolved by the day 9 observation.
CONCLUSION	The notified chemical is slightly irritating to the skin.
TEST FACILITY	Evic-Ceba, (1997b)

B.3. Irritation – eye

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand albino
Number of Animals	3
Observation Period	11 days
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	2	0.7	1.3	2	<11 days	0
Conjunctiva: chemosis	1	0	1	1	<7 days	0
Conjunctiva: discharge	1	0	0.3	3	<6 days	0
Corneal opacity	0.3	0	0	1	<48 hrs	0
Iridial inflammation	0	0	0	1	<24 hrs	0

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

Remarks - Results: No iridial and only slight corneal effects were reported. Moderate conjunctival irritation was noted in treated eyes 1 hour post instillation with treated eyes appearing normal after 11 days.

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

TEST FACILITY: Evic-Ceba (1997c)

B.4. Skin sensitisation

TEST SUBSTANCE: Notified chemical

METHOD: Similar to OECD TG 406 Skin Sensitisation - Magnusson and Kligman guinea pig maximisation test.

Species/Strain: Guinea pig/Dunkin Hartley

PRELIMINARY STUDY: Maximum Non-irritating Concentration:
intradermal: 10%
topical: 100%

MAIN STUDY

Number of Animals: Test Group: 20F Control Group: 10F

INDUCTION PHASE: Induction Concentration:
intradermal: 10%
topical: 100%

Signs of Irritation: Following the intradermal and topical induction phases, minimal-moderate irritation at the induction sites was noted.

CHALLENGE PHASE

1st challenge: topical: 100%

Remarks - Method: No significant protocol deviations.
The vehicle was liquid paraffin.
The test sites were treated with sodium lauryl sulfate prior to the topical induction phase.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: 1st challenge*	
		24 h	*48 h*
Test Group	100%	0	0
Control Group	100%	0	0

Remarks - Results: One test animal was killed in extremis on day 10 of the study and was found to have a prolapsed rectum and the colon was distended with gas. Following the challenge phase, no signs of skin reaction were noted in any of the remaining animals.

CONCLUSION: There was no evidence of reactions indicative of skin sensitisation to the

notified chemical under the conditions of the test.

TEST FACILITY Toxicol (1995)

B.5. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD Similar to OECD TG 471 Bacterial Reverse Mutation Test.
Plate incorporation procedure

Species/Strain *S. typhimurium*: TA1535, TA1537, TA98, TA100
E. coli: WP2uvrA (pKM101) and WP2 (pKM101)

Metabolic Activation System Aroclor 1254-induced rat liver (S9 homogenate)

Concentration Range in Main Test a) With metabolic activation: 0, 1.5, 5, 15, 50, 150 µg/plate
b) Without metabolic activation: 0, 5, 15, 50, 150, 500 µg/plate

Vehicle Dimethyl sulphoxide

Remarks - Method A preliminary toxicity test (0-5000 µg/plate) was performed using all strains to determine the toxicity of the test material.

Vehicle and positive controls were used in parallel with the test material. Positive controls: i) sodium azide (TA1535, TA100), 9-aminoacridine (TA1537), 2-nitrofluorene (TA98), sodium azide (TA100), mitomycin C [WP2(pKM101)] and potassium dichromate (WP2uvrA); ii) with S9: 2-anthramine (TA1535, TA1537, TA98 and TA100) and Benza[a]pyrene [WP2uvrA and WP2(pKM101)].

Test 2 (with metabolic activation) was conducted using the pre-incubation procedure and at the following concentrations: 1.5, 5, 15, 50, 150 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	≥500	>150	>150	Negative
Test 2		>150	>150	Negative
Present				
Test 1	≥500	≥500	>500	Negative
Test 2		≥50	>150	Negative

Remarks - Results In the preliminary toxicity study, the test material was toxic to all bacterial strains at ≥500 µg/plate, with and without metabolic activation. In the mutation study, the material was toxic to all strains at ≥500 or ≥50 (pre-incubation), in the presence of metabolic activation. Thus, the material was tested up to the toxic limit.

No significant increase in the frequency of revertant colonies were noted for any of the bacterial strains up to and including the maximum dose, either with or without metabolic activation.

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

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

TEST FACILITY IPL (1997)

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