File No: LTD/1772

June 2016

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Pamplewood

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (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/1772	Firmenich Ltd	Pamplewood	Yes	≤ 1 tonne per annum	Cosmetic ingredient

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

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 1)	H400 – Very toxic to aquatic life
Chronic (Category 1)	H410 – Very toxic to aquatic life with long lasting effects

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

- 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 skin and eyes

- 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:
  - Coveralls
  - Impervious gloves
  - Eye protection

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 of 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

- Where reuse or recycling are not appropriate, dispose of the notified chemical in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

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 concentration of the chemical exceeds or is intended to exceed 1% in fine fragrances and household products or 0.1% in cosmetic products.

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from cosmetic 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.

No additional secondary notification conditions are stipulated.

(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 Ltd (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, residual monomers, 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, dissociation constant, particle size, flammability limits, explosive properties, oxidising properties, reactivity.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
No

NOTIFICATION IN OTHER COUNTRIES
Canada (NDSL), 2005
China, 2005
EU, 2004
Japan, 2007
Philippines, (PICCS) 2006
Switzerland, 2006
United States (TSCA), 2016

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Pamplewood

MOLECULAR WEIGHT
< 500 Da

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

3. COMPOSITION

DEGREE OF PURITY
> 90%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless to pale yellow liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -20 °C	Measured
Boiling Point	266 °C at 97.6 kPa 261 °C at 97.36 kPa	Measured
Relative density	0.951 at 20 °C	Measured
Vapour Pressure	0.01 kPa at 25 °C	Measured
Water Solubility	7.07×10^{-3} g/L at 20 °C	Measured

Hydrolysis as a Function of pH	Hydrolytically stable	Measured
Partition Coefficient (n-octanol/water)	log Pow = 4.56 - 4.66 at 25 °C	Measured
Adsorption/Desorption	log K_{oc} = 4.02 – 4.14	Estimated (US EPA EPI Suite™ v EPIWIN WSKOW v.I.41). The notified chemical is not expected to significantly adsorb to sediment, sludge or soil based on its low molecular weight and low water solubility
Dissociation Constant	Not determined	The notified chemical does not contain any functional groups that are expected to dissociate in water.
Flash Point	114 °C at 101.3 kPa 116 °C at 101.3 kPa	Measured
Flammability	Not determined	Flashpoint test data indicates that the notified chemical is not a flammable liquid.
Autoignition Temperature	230 °C	Measured
Explosive Properties	Not determined	Not expected to be explosive based on chemical structure.
Oxidising Properties	Not determined	Not expected to be oxidative based on chemical structure.

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 not 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.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported into Australia in its pure form or as a component in a fragrance formula (at a concentration ≤ 5%).

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 notified chemical will be imported in either its pure form or as a component of fragrance preparations containing the notified chemical (at ≤ 5% concentration). The notified chemical will be imported and distributed in tightly closed lacquered drums of 180, 100, 50, 25, 10 or 5 kg in size. They will be transported by road to the Firmenich Ltd warehouse for storage and then distributed to reformulation sites. It is also possible that the notified chemical will be transported directly to the customer's facilities from the port of entry. End-use products will be packaged in containers suitable for retail sale.

USE
The notified chemical is intended to be used as a fragrance ingredient for a variety of cosmetic and household cleaning products (proposed usage concentration ≤ 1% concentration in fine fragrances and household products and ≤ 0.1% in cosmetic products).

OPERATION DESCRIPTION
The procedures for incorporating the imported preparations (in pure form or at ≤ 5% concentration) 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. It is expected that the reformulation processes will involve blending operations that will be highly automated and occur in a fully enclosed/contained environment, followed by automated filling (using sealed delivery systems) of the reformulated end-use products into containers of various sizes.

The end-use products containing the notified chemical (at ≤ 1% concentration) 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
Transportation and Storage
Transport and storage workers may come into contact with the notified chemical, in its pure form or as a component of the imported preparations (at a concentration of ≤ 5%), only in the event of accidental rupture of containers.

Mixing/Blending/Filling/Packaging
During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified chemical (in pure form or at ≤ 5% concentration) may occur during weighing and transfer stages, equipment preparation, blending, quality control analysis and cleaning and maintenance of equipment, Exposure is expected to be minimised through the use of mechanical exhaust ventilation and/or enclosed systems and through the use of personal protective equipment (PPE) such as gloves, respirator, eye protection and uniform.

Drum handling and drum cleaning
Empty drums will be rinsed and re-used, recycled or disposed of in landfill. Worker exposure to the notified chemical in pure form or at ≤ 5% concentration, will be reduced through the use of PPE such as gloves, respirator, eye protection and uniform.

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. hairdressers, workers in beauty salons) or in the cleaning industry. Such professionals may use PPE 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 a concentration ≤ 1%) through the use of the 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.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the following table. For full details of the studies, refer to 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 – non-adjuvant test.	no evidence of sensitisation (75%)
Human, skin sensitisation – RIPT (10%)	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics, metabolism and distribution.

No information on the toxicokinetics of the notified chemical was provided. For dermal absorption, molecular weights below 100 Da. are favourable for absorption and molecular weights above 500 Da. do not favour absorption (ECHA, 2014). Dermal uptake is anticipated to be low to moderate if the water solubility is between 1-100 mg/L and with log P values above 4, the rate of dermal penetration may be limited by the rate of transfer between the stratum corneum and the epidermis, but uptake into the stratum corneum will be high (ECHA, 2014). Based on the water solubility (7.07 mg/L at 20 °C), partition coefficient (log P_{ow} = 4.56 – 4.66) and the moderate molecular weight (100 - 500 Da) of the notified chemical, dermal absorption is expected to be low.

Acute toxicity.

The notified chemical was found to be of low acute toxicity via the oral route.

Irritation and sensitisation.

The notified chemical was determined to be slightly irritating to the skin of rabbits, with well-defined erythema in all animals persisting for up to 72 hours. Slight oedema was noted in all animals, persisting for up to 48 hours with very slight oedema noted in all animals at 72 hours. All animals appeared normal after 7 - 14 days. At 7 days it was noted that adverse reactions including severe desquamation prevented erythema and oedema evaluations. All animals appeared normal after 14 days with no desquamation or other adverse reactions affecting oedema and erythema assessment.

In an eye irritation study in rabbits, mild to moderate conjunctival irritation was noted, with all treated eyes appearing normal within 7 days. One animal showed slight initial pain when dosed with the test substance, and this animal exhibited a longer moderate conjunctival response and recovery period (was the last to show a full recovery) than the other animals in the study.

The notified chemical was not a skin sensitiser when tested in guinea pigs and in a human repeat insult patch study.

Repeated dose toxicity.

No repeated dose toxicity data was provided for the notified chemical. Bicyclo[3.1.1]heptane 6,6-dimethyl-2-methylene-, (1*S*,5*S*)- (CAS No. 18172-67-3) was proposed as an analogue (analogue 1) to the notified chemical. However, as no repeated-dose toxicity data was available for analogue 1, Bicyclo[3.1.1]hept-2-ene 2,6,6-trimethyl (CAS No. 80-56-8) was proposed as another analogue (analogue 2). Repeated-dose inhalation toxicity data is available for analogue 2 and a No Observed Adverse Effect Concentration (NOAEC) was provided.

However, analogues 1 and 2 were not considered sufficiently reliable as analogues to the notified chemical based on their structural differences and much lower molecular weight (half that of the notified chemical).

Mutagenicity/Genotoxicity.
The notified chemical was found to be non-mutagenic in a bacterial reverse mutation assay.

Health hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia, or 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 in its pure form or at ≤ 5% concentration may occur during blending operations. The notified chemical has the potential to cause slight skin and eye irritation. In addition, there is no information on the toxicity of the notified chemical following repeated exposure. Therefore, caution should be exercised when handling the notified chemical during reformulation processes.

However, provided that control measures are in place to minimise worker exposure, including the use of automated processes and PPE, 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 ≤ 1% 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 that 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% in fine fragrances and household cleaning products, and ≤ 0.1% in other cosmetic products, is not considered to be unreasonable.

6.3.2. Public Health

The public will be exposed to the notified chemical at ≤ 1% concentration in fine fragrances and household products and ≤ 0.1% in other cosmetic products. The main route of exposure is expected to be dermal with some potential for accidental ocular or oral exposure.

Local effects
The notified chemical is not expected to be a skin sensitiser based on animal and human studies. The notified chemical is slightly irritating to the eyes and skin. However, skin irritation effects were not observed in human skin sensitisation studies where the notified chemical was regularly applied at a concentration of 10%. At the proposed concentrations of the notified chemical in cosmetic and household products, skin and eye irritation effects are not expected.

Systemic effects
The notified chemical was of low acute toxicity. However, there is no available information on the toxicity of the notified chemical following repeated exposure. Systemic exposure is expected to be limited by the predicted low dermal absorption and the low proposed usage concentration of the notified chemical of ≤ 1% in fine fragrances and household products and ≤ 0.1% in other cosmetic products. In the absence of data on the repeat dose toxicity potential of the notified chemical, use of the notified chemical is supported only under limited exposure conditions, which are reflected in the low concentration of the notified chemical in end-use products.

Therefore the risk associated with the use of the notified at ≤ 1% in fine fragrances, ≤ 0.1% in other cosmetic products and ≤ 1% 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 not be manufactured in Australia; therefore there is no release of the notified chemical to the environment is expected from this activity. Environmental release during importation, transport and distribution may occur as a result of accidental spills. In the event of a spill, the notified chemical is expected to be contained and collected with an inert absorbent material and disposed of in accordance with local regulations.

Release to the environment during blending of the notified chemical into end-use products is expected to be minimal as the blending operation will take place in highly automated and fully enclosed/contained environment with local exhaust ventilation. During blending processes, limited release of the notified chemical is expected from cleaning of equipment as washings will be reused. A total of up to 0.2% of the import volume is estimated to be generated as waste from residues in empty containers and spills during reformulation. Empty containers containing the notified chemical will either be recycled or disposed of through an approved waste management facility.

RELEASE OF CHEMICAL FROM USE

The majority of the notified chemical is expected to be released to sewers across Australia as a result of its use in cosmetic and domestic products. A small percentage of up to 3% of the total import volume of the notified chemical, as residues in empty end use containers, is expected to be disposed of to landfill.

RELEASE OF CHEMICAL FROM DISPOSAL

It is expected that some of the product containing the notified chemical will remain in end-use containers. The containers are expected be disposed of through domestic garbage disposal and will enter landfill, or be subjected to recycling processes.

7.1.2. Environmental Fate

Following its use in Australia, the majority of the notified chemical is expected to enter the sewer 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 a fragrance ingredient in cosmetic and household care products. The notified chemical is not readily biodegradable and, based on its calculated high adsorption coefficient (log Koc = 4.02 – 4.14), low molecular weight and low water solubility, the notified chemical is not expected to significantly adsorb to sediment, sludge or soil.

The results from a photodegradation tests indicates that the notified chemical is intrinsically photolabile through reaction with hydroxyl radicals present in sunlit natural water. It was observed that the notified chemical underwent indirect photodegradation in different environments with half-lives lower than 18 days. The photodegradation products of the notified chemical indicated a mineralisation of the notified chemical when it was reacted with hydroxyl radicals in an aqueous solution. Therefore, the notified chemical is not likely to persist in the aquatic environment. The notified chemical has potential to be bioaccumulative based on its high partition coefficient (4.56 - 4.66). However, it is expected to photodegrade with efficient removal in sewage treatment plants. In surface waters, the notified chemical is expected to photodegrade and eventually degrade through biotic and abiotic processes to form water and oxides of carbon.

The half-life of the notified chemical in air is calculated to be 1.54 hours based on reactions with hydroxyl radicals (AOPWIN v1.92; US EPA, 2011). 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. Notified chemical residues in landfill and soil are expected to be immobile based on its predicted adsorption coefficient (log Koc = 4.02 – 4.14), and are eventually expected to degrade to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The calculation for the predicted environmental concentration (PEC) is summarised in the table below. Based on the reported use in cosmetics and household cleansing products, it is assumed that 100% of the total import

volume of the notified chemical is released to the sewer. The release is assumed to be nationwide over 365 days per year. It is conservatively assumed that 0% of the notified chemical will be removed during sewage treatment processes.

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 - Ocean:	0.06	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1,000 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 1,500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.6 µg/L may potentially result in a soil concentration of approximately 4.038 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 20.2 µg /kg and 40.4 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*
Daphnia Toxicity	48 h EC50 = 0.97 mg/L	Very toxic to aquatic invertebrates

Based on the ecotoxicological endpoint the notified chemical is expected to be very toxic to aquatic invertebrates on an acute basis. Therefore, under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009), the notified polymer is formally classified as "Acute Category 1; Very toxic to aquatic life". Based on the acute toxicity, lack of biodegradability and high bioaccumulation potential of the notified chemical, it is formally classified as "Chronic Category 1; Very toxic to aquatic life with long lasting effects" under the GHS.

7.2.1. Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC) was calculated using the daphnia toxicity endpoint (48 hours, LC50 = 0.97 mg/L) of the notified chemical and a conservative assessment factor of 1000. The most conservative assessment factor of 1000 was used as the ecotoxicity endpoint for only one trophic level was available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (Invertebrates).	0.97	mg/L
Assessment Factor	1,000	
PNEC:	0.97	µg/L

7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) has been calculated for a worst case discharge scenario based on the predicted PEC and PNEC.

Risk Assessment	***PEC µg/L***	***PNEC µg/L***	***Q***
Q - River:	0.61	0.97	0.625

Q - Ocean:	0.06	0.97	0.062

The risk quotient for discharge of treated effluents containing the notified chemical to the aquatic environment (Q < 1) indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in surface waters based on its maximum annual importation quantity. The notified chemical not expected to be readily biodegradable and has the potential to bioaccumulate in the environment. However, the notified chemical is not expected to persist in the environment due to its photodegradability.

Therefore, the notified polymer is unlikely to result in ecotoxicologically significant concentrations in the aquatic environment on the basis of the PEC/PNEC ratio, maximum annual importation volume and assessed use pattern in cosmetic and domestic products.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point < -20 °C

Method	OECD TG 102 Melting Point/Melting Range. EC Directive 92/69/EEC A.1 Melting/Freezing Temperature
Remarks	Determined by placing a test tube containing the test substance in a dry ice/isopropanol mixture until the temperature of the substance reached -20 °C. The test substance remained unchanged in appearance during cooling.
Test Facility	Firmenich (2002) and SafePharm (2003a)

Boiling Point 266 °C at 97.6 kPa and 261 °C at 97.36 kPa

Method	OECD TG 103 Boiling Point. EC Directive 92/69/EEC A.2 Boiling Temperature
Remarks	Determined according to the Siwoloboff method. Second measurement determined by differential scanning calorimetry
Test Facility	Firmenich (2002) and SafePharm (2003a)

Density 0.951 at 20 °C

Method	EC Council Regulation No 440/2008 A.3 Relative Density.
Remarks	Determined by using an oscillating density meter
Test Facility	Firmenich (2002)

Vapour Pressure 0.01 kPa at 25 °C

Method	OECD TG 104 Vapour Pressure. EC Council Regulation No 440/2008 A.4 Vapour Pressure.
Remarks	Boiling temperature verified by Siwoloboff method
Test Facility	Firmenich (2003)

Water Solubility 7.07×10^{-3} g/L at 30 °C

Method	EC Council Regulation No 440/2008 A.6 Water Solubility.
Remarks	Flask Method. Two peaks were observed in the gas chromatography (GC) due to different isomers of the notified chemical.
Test Facility	SafePharm (2003a)

Hydrolysis as a Function of pH Hydrolytically stable

Method	Firmenich S. A Geneva, Internal method.
Remarks	The GC shows the disappearance of the notified chemical after 5 days is less than 10% at any pH (from 2-12) at 40 °C. Therefore, it was concluded that the notified chemical is hydrolytically stable.
Test Facility	Firmenich (2014a)

Partition Coefficient (n-octanol/water) log Pow = 4.56 – 4.66 at 25 °C

Method	OECD TG 123 Partition Coefficient (1-Octanol/Water): Slow Stirring Method.
Remarks	Determined based on the quantifiable isomers present (isomer 1 and 2).
Test Facility	Noack (2015)

Flash Point 116 ± 2 °C at 97.8 kPa and 114 ± 2 °C at 101.3 kPa

Method	EC Council Regulation No 440/2008 A.9 Flash Point.
Remarks	Determined using a closed cup equilibrium method.
Test Facility	Firmenich (2002) and SafePharm (2003b)

Autoignition Temperature 230 ± 2.5 °C

Method	EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases). EC Council Regulation No 440/2008 A.16 Relative Self-Ignition Temperature for Solids.
Remarks	Aliquots of test substance were injected into heated test flask and observed for signs of ignition.
Test Facility	Firmenich (2014b)

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, 6F
- Vehicle: Test substance used as supplied
- Remarks - Method: No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3 F	2000	0/3
2	3 F	2000	0/3

- LD50: > 2000 mg/kg bw
- Signs of Toxicity: Hunched posture was observed in all animals in group 1 at 1 h. Hunched posture and pilo-erection was observed in all group 1 animals at 2 h and 4 h. These effects lasted for 24 h only.

  Hunched posture and pilo-erection was observed in all group 2 animals at 4 h with 1/3 animals in this group exhibiting this effect for more than 24 h.

  All animals (6/6) appeared normal after 48h.
- Effects in Organs: One animal exhibited raised white foci on the non-glandular region of the stomach. No abnormalities were noted at necroscopy of the other animals (5/6).
- Remarks - Results: All animals exhibited satisfactory body weight gain.

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

TEST FACILITY: SafePharm (2003c)

B.2. Irritation – skin

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 404 Acute Dermal Irritation/Corrosion.
EC Directive 2004/73/EC B.4 Acute Toxicity (Skin Irritation).
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 3M
- Vehicle: Test material was used as supplied
- 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	1.67	2	2	2	< 14 days	0
Oedema	1.67	1.33	1.67	2	< 14 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 in all animals persisting for up to 72

hours (2/3 animals).

Slight oedema was noted in all animals, persisting for up to 48 hours (2/3 animals) with very slight oedema noted in all animals at 72 hours.

All animals appeared normal after 7 - 14 days. At 7 days it was noted that adverse reactions including severe desquamation prevented erythema and oedema evaluations. All animals appeared normal after 14 days with no desquamation or other adverse reactions affecting oedema and erythema assessment.

CONCLUSION The notified chemical is slightly irritating to the skin.

TEST FACILITY SafePharm (2003d)

B.3. 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).
EC Directive 2004/73/EC B.5 Acute Toxicity (Eye Irritation).

Species/Strain Rabbit/New Zealand White
Number of Animals 3M
Observation Period 3 days; one rabbit observed for 7 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	1.33	1	0.33	2	< 7 days	0
Conjunctiva: chemosis	0.33	0.33	0.33	2	< 48 hours	0
Conjunctiva: discharge	0.67	0.67	0.33	2	< 72 hours	0
Corneal opacity	0	0	0	0	0	0
Iridial inflammation	0	0	0	0	0	0

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

Remarks - Results One animal showed slight initial pain when dosed with the test substance, and this animal exhibited a longer moderate conjunctival response and recovery period than the other animals in the study.

No corneal or iridial effects were noted during the study.

Moderate conjunctival irritation was noted in all animals 1h after treatment, persisting in 2/3 animals after 24h with the remaining animal showing minimal conjunctival irritation (after 24h). Minimal conjunctival irritation was noted in 2/3 animals after 48h persisting in 1/3 animals up to 72h.

Apparent full recovery was observed in 1/3 animals 48h, 2/3 animals at 72h with the remaining animal appearing normal at 7 days (this was the animal which exhibited the strongest initial pain reaction).

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY SafePharm (2003e)

B.4. Skin sensitisation

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 406 Skin Sensitisation – Magnusson – Kligman Method
Species/Strain	Guinea pig/Hartley albino
PRELIMINARY STUDY	Maximum Non-irritating Concentration: 75% intradermal: 5% topical: 100%
MAIN STUDY	
Number of Animals	Test Group: 20 Control Group: 10
INDUCTION PHASE	Induction Concentration: intradermal: 5% topical: 100%
Signs of Irritation	Test sites were treated with sodium lauryl sulfate 24 hours prior to induction and faint erythema was noted prior to animals in the positive control group and initial negative control group being inducted. Faint erythema was noted at all test sites 1 hour after removal of the patch. Due to technical error, the animals assigned to the initial negative sham control group (referred to as 'sham control group in report) were mistakenly exposed to the test substance during the topical induction phase. These animals were removed from the test. The naïve control group received a single dose of the maximum non-irritating concentration of the notified chemical at challenge only. Intradermal results were not provided.
CHALLENGE PHASE	
1st challenge	topical: 75%
Remarks - Method	Occlusive dressing used in preliminary irritation testing and challenge phase. The positive control used was α-hexylcinnamaldehyde and the results were from a test conducted 10 months earlier. No other significant deviations from the protocol were noted.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: 1st challenge*	
		24 h	*48 h*
Test Group	75%	4/20	0/20
Control Group	75%	4/10	0/10
Sham Control Group	-	-	-

Remarks - Results	The historic positive control gave a satisfactory response confirming the validity of the test system. Faint to moderate erythema was noted in 9/10 animals after 24 hours, with persistence of faint erythema in 7/10 animals at 48 hours. Desquamation was observed at several sites following the challenge phase. Very faint erythema was observed in 4/20 test group animals at 24 hours. All animals were free of irritation at 48 hours. Very faint erythema was also observed in 4/10 animals in the second negative control (naïve) animals. No animals in the test group and negative control groups exhibited an irritancy response greater than very faint.

CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	Product Safety Laboratories (2003)

B.5. Skin sensitisation – human volunteers

TEST SUBSTANCE	Notified chemical (10% in vehicle)
METHOD	Repeated insult patch test with challenge
Study Design	Induction Procedure: Patches containing 0.3 mL test substance were applied to the backs of participants. Patches were removed by the participants after 24 hours. A 24 hour period, during which no test material was applied, followed the weekday patch removals; a 48 hour period followed the weekend patch removals. Each subject returned when required for the reaction to be scored and recorded. The identical test site was then repatched until 9 induction patchings were completed over a 3 week period. Rest Period: 14 days Challenge Procedure: A patch was applied to a naïve site. Patches were removed by laboratory technicians after 24 hours and the sites were scored and recorded. Additional challenge readings were made at 48, 72 and 96 hours post-patch removal.
Study Group	78 F, 28 M; age range 18 - 75 years
Vehicle	75% diethyl phthalate/25% ethanol
Remarks - Method	Occluded. The test substance was applied on a 25 mm Hill Top Chambers® patch.
RESULTS	
Remarks - Results	106/120 subjects completed the study. 11/120 voluntarily withdrew and 3/120 were discontinued for protocol violations. No subject discontinued due to test substance reaction. Two subjects exhibited faint, minimal erythema during the induction phase. Two other subjects exhibited minimal to low-level erythema reactions during the challenge period.
CONCLUSION	The test substance was non-sensitising under the conditions of the test.
TEST FACILITY	Harrison Research (2011)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, TA102
Metabolic Activation System	Mammalian/ S9 fraction
Concentration Range in Main Test	a) With metabolic activation: 5 - 5000 µg/plate b) Without metabolic activation: 5 - 5000 µg/plate
Vehicle	Dimethyl sulphoxide
Remarks - Method	A preliminary toxicity assay (5 – 5000 µg/plate) was performed to determine the toxicity of the test material. The experiment was repeated on a different day using a range of 5 – 1500 µg/plate for TA100, TA1535 and TA1537; and 15 – 5000 µg/plate for TA102 and TA98. Fresh cultures and test substance solutions were used. Additional dose levels were used in both experiments to provide a

minimum of four non-toxic doses.

Vehicle and positive controls were used in parallel with the test material. Positive controls: i) without S9: N-ethyl-N'-nitro-N-nitrosoguanidine (3 µg/plate for TA100 and 5 µg/plate for TA1535), 9-aminoacrridine (80 µg/plate for TA1537), mitomycin C (0.5 µg/plate for TA102) and 4-nitroquinoline-1-oxide (0.2 µg/plate for TA98); ii) with S9: 2-aminoanthracene (1 µg/plate for TA100 and 2 µg/plate for TA1535 and TA1537), benzo(a)pyrene (5 µg/plate for TA98) and 1,8-dihydroxyanthraquinone (10 µg/plate for TA102).

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 1500	≥ 5000	> 5000	Negative
Test 2		≥ 1500	> 5000	Negative
Present				
Test 1	≥ 500	≥ 1500	> 5000	Negative
Test 2		≥ 1500	> 5000	Negative

Remarks - Results

In general, no significant increases in the frequency of revertant colonies were recorded, with or without metabolic activation.

The test material caused a visible reduction in the growth of the bacterial background lawn to all of the tester strains except TA102 both with and without metabolic activation.

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

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

SafePharm Laboratories (2002)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test. Method C.4-C of Commission Directive 92/69/EEC and US EPA Fate, Transport and Transformation Test Guidelines OPPTS 835.3110.
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None reported.
Analytical Monitoring	Dissolved organic carbon (DOC)
Remarks - Method	The test was conducted following the test guideline and good laboratory practice (GLP).

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
10	9	10	56
14	9	14	60
22	10	21	72
28	11	28	85
29	7	29	90

Remarks - Results	All validity criteria were satisfied and no significant deviations to protocol were reported. The notified chemical attained 11% degradation on 28 days.
CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	SafePharm Laboratories (2003f)

C.1.2. Photodegradation

TEST SUBSTANCE	Notified chemical
METHOD	OECD and US EPA guidelines for direct photolysis (OECD 316 and US EPA OPPTS 835.2210 1998a) and for indirect photolysis (US EPA OPPTS 835.5270, 1998b).
Light source and Spectrum	Solar simulator and under natural sunlight
Relative Intensity	5385 MJ/m^2 (Melbourne) and 7236 MJ/m^2 (Townsville)
Remarks – Method	High performance liquid chromatography using Mass Chromatography HPLC-MS. The indirect photodegradation processes were probed to identify the main process responsible and determine its second-order rate constant.
Results	
Remarks - Results	The notified chemical underwent indirect photodegradation in different environments with half-lives lower than 18 days.
Conclusion	The notified chemical is intrinsically photolabile through reaction with hydroxyl radicals present in sunlit natural water.
Test Facility	Firmenich (2015)

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 reported
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	High performance liquid chromatography (HPLC-UV)
Remarks - Method	Twenty animals in test group and control group, divided into 2 replicates (10 animals / replicate) were exposed to an aqueous solution of test substance at 21 °C under static conditions. The test was conducted in accordance with the test guideline without significant deviations. good laboratory practice (GLP) was followed.

RESULTS

Concentration mg/L *Nominal*	*Number of D. magna* (per Replicate)	*Number Immobilised (%)* *24 h [acute]*	*48 h [acute]*
Control	10	0	0
0.13	10	0	0
0.23	10	0	0
0.41	10	0	0
0.73	10	0	0
1.30	10	70	100
2.30	10	100	100
4.10	10	100	100
7.30	10	100	100
13.0	10	100	100

LC50	0.97 mg/L at 48 hours
NOEC (or LOEC)	0.73 mg/L at 48 hours
Remarks - Results	All validity criteria were satisfied and no significant deviations to protocol were reported.
CONCLUSION	The notified chemical is very toxic to aquatic invertebrates.
TEST FACILITY	SafePharm Laboratories (2004)

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