File No: LTD/1576

May 2012

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Jasmonitrile

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:

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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 SUBSTANCE	INTRODUCTION VOLUME	USE
LTD/1576	Firmenich Limited	Jasmonitrile	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 classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).with the following risk phrases: R38 Irritating to skin. R22 Harmful if swallowed

and

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*
Acute toxicity	Category 4	Harmful if swallowed
Skin Corrosion/Irritation	Category 2	Causes skin irritation
Aquatic Environment	Acute Category 2 Chronic Category 2	Toxic to aquatic life Toxic to aquatic life with long lasting effects

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

- Safe Work Australia, should consider the following health hazard classification for the notified chemical:
  - Xn: R22 Harmful if swallowed
  - Xi: R38 Irritating to skin

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - Conc. ≥25%: Xn; R22; R38;
  - ≥20% Conc. <25%: Xi; R38.

- 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

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical during reformulation processes:
  - Enclosed, automated processes, where possible
  - Ventilation system including local exhaust ventilation

- 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
  - Avoid inhalation of vapours

- 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

  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;
  - information associated with the repeated dose and/or inhalation toxicity of the notified chemical becomes available;
  - the concentration of the chemical exceeds or is intended to exceed 0.001% in fine fragrances, 0.01% in other cosmetic products and 0.5% 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.

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

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, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, impurities and additives/adjuvant.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: density, vapour pressure, hydrolysis as a function of pH, adsorption/desorption, flammability and autoignition temperature.

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

NOTIFICATION IN OTHER COUNTRIES
USA (1998), Philippines (2000), Canada (2004), Switzerland (2006),

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Jasmonitrile

MOLECULAR WEIGHT
<500 Da

ANALYTICAL DATA
Reference NMR, IR, GC, MS 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	<-20 ºC	Measured
Boiling Point	218 ºC at 99.88 kPa	Measured
Density	810-818 kg/m^3 at 20 ºC	MSDS
Vapour Pressure	1.2 x 10^{-2} kPa at 20 ºC	Measured. Study report not provided in English.
Water Solubility	2.92 × 10^{-2} g/L at 20 ºC	Measured (using method A6 of Commission Directive 92/69/EEC)
Hydrolysis as a Function of pH	≤15% (pH 2-12) at 40 ºC, 28 days	Measured
Partition Coefficient (n-octanol/water)	log Kow >3.49 at 21-22 ºC	Measured (using method A8 of Commission Directive 67/548/EEC). Calculated log Kow = 3.71 (KOWWIN, v1.68; US EPA, 2009)
Adsorption/Desorption	log K_{oc} = 2.72 (MCI Method) log K_{oc} = 3.25 (Kow Method)	Calculated (KOCWIN v2.00, from MCI and log Kow, US EPA, 2009)
Dissociation Constant	Not determined	Not expected to be ionised in the environmental pH range (4-9)
Flash Point	90 ºC at 101.3 kPa (closed cup)	Measured. Classified as a C1 combustible liquid (NOHSC, 2001).
Flammability	Not determined	Based on the flash point, not classified as flammable (NTC, 2007)
Autoignition Temperature	>90 ºC based on flash point	Not expected to autoignite under normal conditions
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 (≤1%) of 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 ≤1% 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 domestic products (proposed usage concentration: ≤0.001% concentration in fine fragrances, ≤0.01% in other cosmetic products and ≤0.5% in household cleaning products).

OPERATION DESCRIPTION
The procedures for incorporating the imported products (containing ≤1% notified chemical) into end-use products will likely vary depending on the nature of the cosmetic and 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 products into containers of various sizes.

The finished 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 products or end-use products (≤1%), only in the event of accidental rupture of containers.

During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified chemical (at ≤1% 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 ≤0.5% 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 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 ≤0.5% 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 2,000 mg/kg bw; harmful
Rabbit, skin irritation	irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – maximisation test	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vivo mouse micronucleus assay	non genotoxic

Toxicokinetics, metabolism and distribution.
Based on the water solubility (2.92 x 10^{-2} g/L at 20 ºC), partition coefficient (log P_{ow} = >3.49 at 20 ºC) 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 harmful in an acute oral toxicity study in rats, with 5/10 animals in the high dose (2,000 mg/kg bw) treatment group found dead two days after dosing. Signs of toxicity noted in animals of this group included ataxia, dehydration, emaciation, hunched posture, lethargy, increased lacrimation, pilo-erection, decreased respiratory rate, laboured respiration, loss of righting reflex and tiptoe gait. At necropsy effects in the liver, lungs, spleen, kidneys, stomach and small intestine were noted.

Acute dermal and inhalation toxicity data were not provided for the notified chemical.

Irritation and Sensitisation.
The notified chemical was determined to be irritating to the skin of rabbits, with well-defined erythema and very slight to slight oedema noted. Slight desquamation was noted in all animals at the end of the observation period.

In an eye irritation study in rabbits, very mild conjuctival irritation was noted with treated eyes appearing normal after 24 hours.

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

Repeated Dose Toxicity.
No repeated dose toxicity data were provided for the notified chemical.

Mutagenicity.
The notified chemical was found to be non-mutagenic in a bacterial reverse mutation assay and was not clastogenic in an in vivo mouse micronucleus test.

Health hazard classification
Based on the data provided, the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrases: R38 Irritating to skin.
R22 Harmful if swallowed

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Reformulation
Exposure of workers to the notified chemical (at ≤1% concentration) may occur during blending operations. While the notified chemical was found to be harmful to human health via the oral route and irritating to the skin, ingestion is unlikely under the occupational settings described and irritant effects are not expected at the proposed introduction and usage concentrations. Given the absence of toxicity studies, particularly related to repeated dose toxicity and the potential toxicity via the inhalation route, steps should be taken to avoid exposure to the notified chemical. Therefore, provided that control measures are in place to minimise worker exposure, including the use of ventilated environments, 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 ≤0.5% 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 ≤0.001% in fine fragrances, ≤0.01% in other cosmetic products and ≤0.5% in household cleaning products, is not considered to be unreasonable.

6.3.2. Public Health
At the proposed usage concentration of the notified chemical of ≤0.001% in fine fragrances, ≤0.01% in other cosmetic products and ≤0.5% 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 ≤0.001% in fine fragrances, ≤0.01% in other cosmetic products and ≤0.5% 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 (≤1%) for local reformulation into a variety of consumer products (cosmetics, household products, fine fragrance). Releases during the reformulation processes at various sites throughout Australia are expected to be limited to traces of spills, formulation equipment cleaning and residues in empty packaging. Less than 0.1% of the total annual import volume of notified chemical is expected to remain as residues in import containers. The empty containers will eventually be recycled or disposed of to landfill. At the end of the reformulation run the formulating and packing equipment will be washed and it is anticipated that the washings will be included in the next batch.

Accidental spills during transport or reformulation are expected to be collected with inert material and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE
The notified chemical is expected to be released to the sewer in domestic situations across Australia as a result of its use in cosmetic, toiletries and household 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 consumer containers are likely to be disposed of through domestic garbage disposal and enter landfill or be recycled.

7.1.2. Environmental Fate

The notified chemical is volatile and may volatilise to air during use or sewage treatment. The half-life of the notified chemical in air is calculated to be 14.5 h based on reaction 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 air compartment.

The majority of the notified chemical will enter the sewer system as a result of the use of this chemical as a component of fragrance preparations, such as cosmetic and household cleaning products. The notified chemical is not readily biodegradable (30% biodegradation after 28 days, OECD TG 301F) and, based on its low adsorption coefficient (log K_{OC} = 2.7-3.2), only limited partitioning to sludge is expected. Most of the notified chemical is expected to remain in the water phase, due to its moderate water solubility (0.0292 g/L at 20 ^{o}C), and may be released from sewage treatment plants to receiving waters, where it will disperse and eventually degrade. It has a low potential to bioaccumulate based on its low bioconcentration factor (log BCF = 2.11), predicted by a regression-based method using an estimated log Kow, as the measured log Kow result is only a lower limit (BCFBAF v3.00; log Kow = 3.71, KOWWIN; US EPA, 2009). A significant proportion of the notified chemical may be applied to land when effluent is used for irrigation, and residues in empty containers are expected to be disposed of to landfill. The notified chemical in landfill, soil and sludge is likely to be relatively mobile. The notified chemical is expected to degrade through biotic or abiotic processes to form water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

Since most of the polymer will be washed into the sewer, under a worst case scenario, with no removal of the notified polymer in the sewage treatment plant (STP), 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	1000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1000	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	0%	Mitigation
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

The notified chemical that is not removed from waste water during STP processes may be released to the environment in STP effluent. STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.606 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

No ecotoxicity data were submitted. As there is the potential for high aquatic exposure from the use and disposal of the notified chemical, reliable modelled estimates for ecotoxicological endpoints for the notified chemical were calculated (ECOSAR (v1.00), neutral organics class, KOWWIN estimated log Kow = 3.71; US EPA, 2009) and are tabulated below.

Endpoint	*Result*	*Assessment Conclusion*
Acute Toxicity		
Fish	96 h LC50 = 3.70 mg/L	Predicted to be toxic to fish
Daphnia	48 h LC50 = 2.69 mg/L	Predicted to be toxic to aquatic invertebrates

Algae	96 h EC50 = 2.68 mg/L	Predicted to be toxic to algae
Chronic Toxicity	ChV = 0.43 mg/L ChV =	
Fish Daphnia	0.41mg/L	Predicted to be toxic to fish with long lasting effects
Algae		Predicted to be toxic to aquatic invertebrates with
	ChV = 1.36mg/L	long lasting effects
		Predicted to be not harmful to green algae with long lasting effects

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 toxic to fish, 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, is greater than the NOEC. On the basis of its lack of ready biodegradability and the ChV endpoints the notified chemical is, at best, toxic with long lasting effects to fish and aquatic invertebrates but not harmful to algae with long lasting effects. In the absence of experimental data, the long-term hazard of the notified chemical is formally classified under the GHS on the basis of its predicted chronic toxicity to aquatic biota, and lack of readily biodegradability, as 'Chronic Category 2: Toxic 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 estimated chronic daphnia toxicity of the notified chemical and an assessment factor of 50. A more conservative assessment factor of 50 is appropriate, in this case, as although chronic endpoints (ChV = (LOEC × 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 (*Daphnia magna*)	0.41 mg/L
Assessment Factor	50
PNEC:	8.20 µg/L

7.3. Environmental Risk Assessment

Based on the above PEC and PNEC, the following Risk Quotient has been calculated.

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.61	8.2	0.074
Q - Ocean	0.06	8.2	0.007

The risk quotient for discharge of effluents containing the notified chemical to the aquatic environment, assuming a worst case with no removal during sewage treatment plant (STP) processes, 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 has a low potential for bioaccumulation and is unlikely to be persistent in the environment. 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 considered to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point <-20 ºC

Method EC Directive 92/69/ECC method A1 Melting Point
Remarks Determined by placing a test tube containing the test substance in a dry ice/acetone bath until the temperature of the substance reached ~-20 ºC. The test substance did not show any indication of freezing.
Test Facility Safepharm (1998a)

Boiling Point 218 ºC at 99.88 kPa

Method EC Directive 92/69/ECC method A2 Boiling Point
Remarks Determined by differential scanning calorimetry (DSC).
Test Facility Safepharm (1998a)

Hydrolysis as a Function of pH <15% (pH 2-12) at 40 ºC, 28 days

Method In-house Stability Test of Perfumery Raw Materials

pH	*% hydrolysis after 7 days at 40 ºC**	*% hydrolysis after 28 days at 40 ºC**
2	≤5	<10
5	≤5	<10
7	≤5	<10
8.5	≤5	<10
12	≤5	<15

*Data points are approximated from the provided graph

Remarks Notified chemical (200 – 300 ppm) 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, 7, 15, 21 and 28.
The hydrolysis was approximately ≤15% for pH range (2-12) after 28 days at 40 ºC. This indicates that the notified chemical has limited potential to hydrolyse under environmental conditions.
Test Facility Firmenich (2011)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 420 Acute Oral Toxicity – Fixed Dose Procedure.
- Species/Strain: Rat/Sprague-Dawley CD
- Vehicle: None
- Remarks - Method: Preliminary study at 500 (1M/1F) and 2000 (1M/1F) conducted to establish the dosage regimen.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	5M, 5F	2000	5/10
II	5M, 5F	500	0/10

- LD50: 2,000 mg/kg bw (discriminating dose 500 mg/kg bw)
- Remarks - Results: The mortalities (3M, 2F) were noted on day 2.
- Signs of Toxicity: Ataxia, dehydration, emaciation, hunched posture, lethargy, increased lacrimation, pilo-erection, decreased respiratory rate, laboured respiration, loss of righting reflex and tiptoe gait were noted in Group I treated animals. Surviving animals recovered by day 5.

  Hunched posture was noted in all female Group II animals, which resolved by day 2. No signs were noted in male Group II treated animals.
- Effects in Organs: Effects noted in animals that died during the study included haemorrhagic lungs, dark or patchy pallor of the liver, pale spleen, dark kidneys, pale gastric mucosa, haemorrhage or sloughing of the non-glandular epithelium of the stomach and haemorrhage of the small intestine.

CONCLUSION: The notified chemical is harmful via the oral route.

TEST FACILITY: Safepharm (1998c)

B.2. Irritation – skin

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 404 Acute Dermal Irritation/Corrosion.
- Species/Strain: Rabbit/New Zealand White
- 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	2	2	2	2	<7 days	0
Oedema	2	1	2	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 and very slight to slight oedema were noted at up to the 72 hour observation. These effects were resolved by the day 7

observation. In addition, a loss of skin elasticity and/or flexibility was reported (at the 72-hour observation) in all animals. Crrust formation was noted at the treated sites of all animals on day 7, with slight desquamation observed at the end of the observation period.

CONCLUSION The notified chemical is irritating to the skin

TEST FACILITY Safepharm (1998d)

B.3. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3
Observation Period 72 hours
Remarks - Method One drop of the local anaesthetic (proxymetacaine hydrochloride, 0.5%) was instilled into both eyes of the second and third animals 1-2 minutes before treatment.

RESULTS

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

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

Remarks - Results No corneal or iridial effects were reported. Slight conjunctival irritation was noted in the treated eyes of two animals 1 hour post instillation. The treated eyes appeared normal after 24 hours.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY Safepharm (1998e)

B.4. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD OECD TG 406 Skin Sensitisation - Maximisation
Species/Strain Guinea pig/Albino Dunkin Hartley
PRELIMINARY STUDY Mild-moderate irritating Concentration:
intradermal: 25%
topical: 100%
MAIN STUDY
Number of Animals Test Group: 20M Control Group: 10M
INDUCTION PHASE Induction Concentration:
intradermal: 25%
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% and 75%
Remarks - Method No significant protocol deviations.
The vehicle was arachis oil BP.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: 1st challenge*	
		24 h	*48 h*
Test Group	100%	0	0
	75%	0	0
Control Group	100%	0	0
	75%	0	0

Remarks - Results: Following the challenge phase, no signs of skin reaction were noted in any of the animals.

CONCLUSION: There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY: Safepharm (1997)

B.5. Genotoxicity – bacteria

TEST SUBSTANCE: Notified chemical

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

Species/Strain: *S. typhimurium*: TA1535, TA1537, TA98, TA100
E. coli: WP2uvrA$^-$

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

Concentration Range in Main Test: a) With metabolic activation: 5, 15, 50, 150, 500, 1500, 5000 µg/plate
b) Without metabolic activation: 5, 15, 50, 150, 500, 1500, 5000 µg/plate

Vehicle: Dimethyl sulphoxide

Remarks - Method: A preliminary toxicity test (0-5000 µg/plate) was performed to determine the toxicity of the test material (TA100 and WP2uvrA$^-$ only).

Vehicle and positive controls were used in parallel with the test material. Positive controls: i) without S9: N-ethyl-N'-nitro-N-nitrosoguanidine (TA100, TA1535, WP2uvrA$^-$), 9-aminoacridine (TA1537) and 4-nitroquinoline-1-oxide (TA98); ii) with S9: 2-aminoanthracene (TA100, TA1535, TA1537, WP2uvrA$^-$) and benzo(a)pyrene (TA98).

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	≥500	≥5000	Negative
Test 2		≥500	≥5000	Negative
Present				
Test 1	≥500	≥500	≥5000	Negative
Test 2		≥500	≥5000	Negative

Remarks - Results: In the preliminary toxicity study, the test material was toxic to the TA100 strain at ≥500 µg/plate with and without metabolic activation and was non-toxic to the WP2uvrA$^-$ strain.

In the mutation studies, the test substance caused a visible reduction in the growth of the bacterial background lawn to all strains (exception

WP2uvrA$^-$), from 500 µg/plate, with and without metabolic activation. Thus, the material was tested up to the toxic limit.

No significant increases in the frequency of revertant colonies were recorded 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 Safepharm (1998f)

B.6. Genotoxicity – in vivo

TEST SUBSTANCE Notified chemical

METHOD OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
Species/Strain Mouse/HSD: ICR
Route of Administration Oral – gavage
Vehicle Arachis oil
Remarks - Method A preliminary toxicity study was conducted, using i) 1 male and 1 female mouse at 1,000 and 2,000 mg/kg bw; and ii) using 2 male mice at 1,600 and 2,000 mg/kg bw. Clinical signs were observed from 1,600 mg kg/bw and a single animal treated at 2,000 mg/kg bw was killed *in extremis*. Therefore, the maximum tolerated dose for the main study was determined to be 1,600 mg/kg bw.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control) x 2	7M	-	24, 48
II (low dose)	7M	400	24
III (mid dose)	7M	800	24
IV (high dose) x 2	7M	1,600	24,48
V (positive control, CP)	5M	50	24

CP=cyclophosphamide

RESULTS
Doses Producing Toxicity There were no mortalities. Signs of toxicity noted in animals in the mid- and high-dose groups included hunched posture, ataxia, lethargy, ptosis and splayed gait.
Genotoxic Effects A statistically significant increase in micronucleated PCEs was not observed at any dose level. The positive control induced statistically significant increases in micronucleated PCEs.
Remarks - Results The authors considered that the observation of clinical signs indicated that systemic absorption had occurred and that the chemical had reached the target tissue.

CONCLUSION The notified chemical was not clastogenic under the conditions of this in vivo Mammalian Erythrocyte Micronucleus Test.

TEST FACILITY Harlan (2009)

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