File No: LTD/1790

November 2014

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Thuyacetone

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/1790	Firmenich Limited	Thuyacetone	Yes	≤ 1 tonne per annum	Fragrance ingredient

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

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

Based on the available information, the notified chemical is not recommended for classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

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.

Based on the available information, when used at ≤ 1.5% in air fresheners or ≤ 0.25% in cosmetics and other household products, 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

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Flammable Liquids (Category 4): H227 – Combustible liquid

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

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical during reformulation:
  - Enclosed, automated processes, where possible
  - Ventilation system including local exhaust ventilation

- 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:
  - Avoid contact with skin and eyes
  - Avoid inhalation

- 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:
  - Impervious gloves, eye protection and coveralls

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

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

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

Public Health

- The following measures should be taken to minimise public exposure to the notified chemical:
  - The notified chemical should only be used at ≤ 1.5% in air fresheners or ≤ 0.25% in cosmetics and other household products.

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 containment, physical 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 notified chemical exceeds or is intended to exceed 1.5% in air fresheners or 0.25% in cosmetics and other household products;
- information becomes available on the repeated dose toxicity of the notified chemical.

or

(2) Under Section 64(2) of the Act; if

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

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

(Material) Safety Data Sheet

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

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Firmenich Limited (ABN: 86 002 964 794)
73 Kenneth Road
Balgowlah NSW 2093

NOTIFICATION CATEGORY
Limited-small volume: Chemical other than polymer (1 tonne or less per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, other names, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, impurities, additives/adjuvants and use details.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: adsorption/desorption, dissociation constant, flammability, explosive properties and oxidising properties

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
USA (2014)
Canada (2006)
Philippines (2006)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Thuyacetone

MOLECULAR WEIGHT
< 200 Da

ANALYTICAL DATA
Reference NMR, IR, 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 liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -20 °C	Measured
Boiling Point	205 °C at 97.5 kPa	Measured
Relative Density	0.897 at 20 °C	Measured
Vapour Pressure	4.2×10^{-2} kPa at 25 °C	Measured
Water Solubility	0.564 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	After 28 days (40 °C) 10% Degradation (pH 2-5) 7.26% Degradation (pH 8.5) 33% Degradation (pH 12)	Measured
Partition Coefficient	log Pow = 2.98 at 20 °C	Measured

(n-octanol/water)		
Adsorption/Desorption	log K_{oc} = 2.77	Calculated (using KOCWIN v2.00; US EPA, 2009)
Dissociation Constant	Not determined	Contains no dissociable functionality.
Flash Point	73 °C at 101.3 kPa	Measured
Autoignition Temperature	> 220 °C	Measured
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidative properties

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

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

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

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

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. The notified chemical will be imported into Australia in the neat form to be reformulated into fragrance formula, as a component of fragrance formula (at ≤ 5% concentration) to be blended into end-use cosmetic and household products, or as a component of end-use cosmetic and household products (at ≤ 1.5% concentration in air fresheners or at ≤ 0.25% concentration in cosmetics and other household products).

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 Limited

TRANSPORTATION AND PACKAGING
The notified chemical, either in its neat form or as a component in a fragrance formula, will be imported and distributed in lacquered drums of varying sizes between 180 kg and 5 kg. The end-use products will be packaged in typical consumer-sized containers suitable for retail sale.

From the port of entry, the notified chemical will be transported by to warehouses where it will be unloaded and stored in its original packaging until further distribution to customer reformulation sites. Alternatively the notified chemical and products containing it will be transported directly from the port of entry to the customer facilities.

USE
The notified chemical is a fragrance ingredient that will be used in consumer products ranging from cosmetics (leave-on and rinse-off products and fine fragrances) to household products (at ≤ 1.5% concentration in air fresheners or at ≤ 0.25% concentration in cosmetics and other household products).

OPERATION DESCRIPTION
At customer sites the notified chemical will be reformulated into either fragrance formula or finished end-use cosmetic/household products. The fragrance formula will be used for further reformulation of consumer products.

The procedures for reformulating the notified chemical or the fragrance formula containing the notified chemical will likely vary depending on the nature of the cosmetic/household products, and may involve both automated and manual transfer steps. In general, it is expected that the reformulation processes will involve blending operations that will normally be automated and occur in an enclosed system, followed by automated filling of the finished products into consumer 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 products, these could be applied in a number of ways, such as by hand, using an applicator or by spray.

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	Unknown	Unknown
Mixing	4	2
Drum handling	4	2
Drum cleaning	4	2
Maintenance	4	2
Quality control	0.5	1
Packaging	4	2

EXPOSURE DETAILS
Transport and storage workers may come into contact with the notified chemical, either in neat form or at various concentrations (in intermediate fragrance formulae and finished consumer products), only in the event of accidental rupture of packaging.

At reformulation sites, dermal, ocular and inhalation exposure of workers to the notified chemical (up to 100% concentration) may occur when handling the notified chemical or products containing it. Exposure is expected to be minimised through the use of mechanical ventilation and/or enclosed systems and through the use of personal protective equipment (PPE) such as coveralls, safety glasses and impervious gloves.

Dermal, ocular and inhalation exposure to the notified chemical in the finished end-use products (at ≤ 1.5% concentration in air fresheners or at ≤ 0.25% concentration in cosmetics and other household products) may occur where workers provide services involving the application of products to clients (e.g. hair dressers, beauty salon workers) or in the cleaning industry. Such workers may use some 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 ≤ 1.5% concentration in air fresheners or at ≤ 0.25% concentration in cosmetics and other household products) through the use of a wide range of cosmetic and household products. The principal routes of exposure will be dermal, while ocular and inhalation exposures (e.g. through the use of spray products) are also possible.

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 > 2,000 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
Human, skin sensitisation – RIPT (30%)	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics, metabolism and distribution.

Based on the water solubility (0.564 g/L at 20 ºC), partition coefficient (log P_{ow} = 2.98) and the low molecular weight (< 500 Da) of the notified chemical, passive diffusion across the gastrointestinal (GI) tract and dermal absorption could occur. The notified chemical may also be absorbed across the respiratory tract.

Acute toxicity.

In a study conducted in rats the notified chemical was found to have low acute oral toxicity.

Irritation and sensitisation.

Based on studies conducted in rabbits the notified chemical was slightly irritating to the skin and eyes.

The notified chemical at concentrations up to 75% in a guinea pig Magnusson & Kligman maximisation study showed no evidence of skin sensitisation.

Repeated dose toxicity.

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

Mutagenicity/Genotoxicity.

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

Health hazard classification

Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System for the 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

Workers may experience dermal, ocular and perhaps inhalation exposure to the notified chemical (at ≤ 100% concentration) during reformulation processes (and during sampling and quality control processes at storage sites). The notified chemical is considered to be a slight skin and eye irritant. The notified chemical was of low acute toxicity, however due to a lack of repeated dose toxicity, harmful effects following repeated exposure to the notified chemical cannot be ruled out. Therefore, caution should be exercised when handling the notified chemical during reformulation processes.

Provided that control measures stated by the notifier 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 may come into contact with products containing the notified chemical (at ≤ 1.5% concentration in air fresheners or at ≤ 0.25% concentration in cosmetics and other household products). These products will also be available to the public. The risk to workers who regularly use these products is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified chemical (for details of the public health risk assessment, see Section 6.3.2).

6.3.2. Public Health

Irritation
The notified chemical is slightly irritating to eyes and the skin. However, irritation effects are not expected from use of the notified chemical at the proposed use concentrations in cosmetic and household products.

Repeat dose toxicity
The repeated dose toxicity effects of the notified chemical have not been determined. However, exposure is expected to be limited by the low concentrations of the notified chemical in end use products.

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at ≤ 1.5% concentration in air fresheners or at ≤ 0.25% concentration in cosmetics and other household products, is not considered to be unreasonable. 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.

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% or up to 2 kg of the import volume is estimated to be released to landfill as a result of reformulation in Australia.

RELEASE OF CHEMICAL FROM USE
The notified chemical is expected to be released to sewers in domestic situations across Australia as a result of its use in cosmetic and domestic products, which are either washed off the hair and skin of consumers, or disposed of following cleaning activities.

RELEASE OF CHEMICAL FROM DISPOSAL
It is estimated that a maximum of 3% or up to 30 kg of the notified chemical will remain in end-use containers. These will be disposed of through domestic garbage disposal and will enter landfill or be recycled.

7.1.2. Environmental Fate
Following its use in Australia, the majority of the notified chemical is expected to enter the sewer system before potential release to surface waters on a nationwide basis. The notified chemical will enter the sewer system as a result of the use of this chemical as component of cosmetics, household products and fine fragrances. The notified chemical is not readily biodegradable and, based on its calculated adsorption coefficient (log Koc = 2.77), partial partitioning to sludge is expected. As only partial adsorption to sludge is expected, release to surface water may occur. The notified chemical is not likely to bioaccumulate due to its n-octanol/water partition coefficient (log Pow = 2.98). In surface waters, the notified chemical is expected to disperse and degrade through biotic and abiotic processes to form water and oxides of carbon.

The notified chemical is moderately volatile from water (log H = 0.4 Pa/m^3/mol; European Commission, 2003) and may slowly volatilise to air during use or sewage treatment. The half-life of the notified chemical in air is calculated to be 7 h, based on reactions with hydroxyl radicals (AOPWIN v1.92; US EPA, 2009). Therefore, the notified chemical is not expected to persist in the air compartment.

A proportion of notified chemical may be applied to land when effluent is used for irrigation or when sewage sludge is used for soil remediation, or disposed of to landfill. Notified chemical residues in landfill, soil and sludge are expected to have low mobility based on its predicted soil adsorption coefficient (log K_{oc} = 2.77) and is expected to eventually degrade to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

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

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	0%	
Daily effluent production:	4,523	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.61	µg/L
PEC - Ocean:	0.06	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.606 µg/L may potentially result in a soil concentration of approximately 4.039 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 20.19 µg/kg and 40.39 µg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity data were submitted. As there is the potential for high aquatic exposure from the use and disposal of the notified chemical, modelled estimates for ecotoxicological endpoints for the notified chemical were calculated using (ECOSAR (v4.00), using the class specific for the functional groups the notified chemical contains and the user entered log Kow = 2.98. The endpoints are tabulated below.

Endpoint	*Result*	*Assessment Conclusion*
Acute Toxicity		
Fish	96 h LC50 = 16.7 mg/L	Predicted to be harmful to fish
Daphnia	48 h EC50 = 10.38 mg/L	Predicted to be harmful to aquatic invertebrates
Algal	96 h EC50 = 11.24 mg/L	Predicted to be harmful to alga

The modelled endpoints used here were derived from the ECOSAR, using a class that was the best fit for the notified chemical, and are considered useful to provide a general indication of potential environmental effects for the notified chemical. However, the number of chemicals in the training set used to develop the ECOSAR class is considered to be insufficient to confidently classify the notified chemical. Therefore, these modelled endpoints are not considered sufficient to formally classify the acute and long term hazard of the notified chemical under the Globally Harmonised System for the Classification and Labelling of Chemicals (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) has been calculated from the estimated acute daphnia toxicity of the notified chemical and an assessment factor of 500. A more conservative assessment factor of 500 is appropriate, in this case, as although acute endpoints for three trophic levels are available as a general indication of potential toxicity, these endpoints are modelled estimates from a classed-based model which has a low number of chemicals in the training sets.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment	
Acute Algal Toxicity	10.38 mg/L
Assessment Factor	500

PNEC:	20.76 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	20.76	0.029
Q - Ocean	0.06	20.76	0.003

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 in surface waters based on its maximum annual importation quantity. Whilst the notified chemical may be persistent in the environment due to its hydrolytic stability, and a lack of ready biodegradability, the notified chemical has a low potential for bioaccumulation. 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.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point < -20 °C

Method OECD TG 102 Melting Point/Melting Range.
Remarks Determined using a temperature sensor.
Test Facility Firmenich (2003)

Boiling Point 205 ± 0.5 °C at 97.5 kPa

Method OECD TG 103 Boiling Point.
Remarks Determined using a temperature sensor.
Test Facility Firmenich (2003)

Relative Density 0.897 at 20 ± 0.5 °C

Method OECD TG 109 Density of Liquids and Solids.
Remarks Determined by changes of the resonance frequency of an oscillator.
Test Facility Firmenich (2003)

Vapour Pressure 4.2×10^{-2} kPa at 25 °C

Method Similar to OECD TG 104 Vapour Pressure.
Remarks Determined using a vapour pressure balance system.
Test Facility Firmenich (2014a)

Water Solubility 0.564 g/L at 20 °C

Method Method A.6 of Commission Directive 92/96/EEC Water Solubility.
Remarks Flask Method
Test Facility Safepharm (2003)

Hydrolysis as a Function of pH After 28 day, 40°C
10% Degradation (pH 2-5)
7.26% Degradation (pH 8.5)
33% Degradation (pH 12)

Method In-house

pH	*T (°C)*	*% hydrolysis after 28 days*
2	40	10
5	40	10
8.5	40	7.26
12	40	33

Remarks Test substance (200 – 300 ppm) was dissolved in buffer solutions (types A, C, D, F and I: Reference Handbook of Chemistry and Physics) containing 1% non-ionic surfactant (Arkopal N 150) and put into storage in an oven at 40 °C over 28 days. Aliquots of test solution were extracted with organic solvent (typically cyclohexane or ethyl acetate) containing a hydrocarbon standard (typically C12, C17 or C20) on a regular basis throughout the test and analysed by GC-FID. After 28 days at 40°C the rate of hydrolysis was 10% at pH 2-5, 7.26% at pH 8.5 and 33% at pH 12. The graph shows that the disappearance of the test substance after 5 days is less than 10% at any pH (from 2 to 12) at 40°C. It can be concluded that under the conditions of the test, the test substance is hydrolytically stable.
Test Facility Firmenich (2014b)

Partition Coefficient (n-octanol/water) log Pow = 2.98 at 40 °C

Method	Method A.8 of Commission Directive 92/69 Partition Coefficient.
Remarks	HPLC Method
Test Facility	Safepharm (2003)

Flash Point 73 ± 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 (2003)

Autoignition Temperature > 220 °C

Method	Not specified
Remarks	Analysis performed in the Firmenich FIRELAB instrument.
Test Facility	Firmenich (2004)

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 (Crl:CD(SD) IGS BR)
- Vehicle: None
- Remarks - Method: No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	6 F	2000	0/6

- LD50: > 2000 mg/kg bw
- Signs of Toxicity: Hunched position, lethargy and ataxia were noted in 3/6 animals.
- Effects in Organs: No abnormalities were noted at necropsy.
- Remarks - Results: All animals showed expected bodyweight gains.

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

TEST FACILITY: SafePharm (2004a)

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: 7 days
- Type of Dressing: Semi-occlusive.
- Remarks - Method: No significant protocol deviations.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	1	1	0.7	1	< 7 days	0
Oedema	0.3	0	0.3	1	< 48 hours	0

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

- Remarks - Results: Very slight erythema was noted at all treated skin sites after 48 hours and at 2/3 treated skin sites after 72 hours. All treated skin sites appeared normal at the 7 days observation. Very slight oedema was noted at 2/3 treated skin sites after 24 hours. All treated skin sites appeared normal at the 7 days observation.

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

TEST FACILITY: SafePharm (2004b)

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 14 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	0	0	2	2	< 14 days	0
Conjunctiva: chemosis	0	0	1	1	< 7 days	0
Conjunctiva: discharge	0	0	1.7	2	< 7 days	0
Corneal opacity	0	0	0.7	1	< 7 days	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 Minimal to moderate conjunctival irritation was noted in all treated eyes 1 hour after treatment. Moderate conjunctival irritation was noted in 1 treated eye at the 24, 48 and 72-hour observations with minimal conjunctival irritation at the 7-day observation.

Scattered or diffuse corneal opacity was noted in 1 treat eye at the 48 and 72-hour observations.

No iridial inflammation was noted.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY SafePharm (2004c)

B.4. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD OECD TG 406 Skin Sensitisation – Magnusson & Kligman Maximisation.
Species/Strain Guinea pig/ albino Dunkin Hartley
PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: 1% and 5% v/v in arachis oil BP
topical: 25%, 50% and 75% in arachis oil BP and 100%
MAIN STUDY
Number of Animals Test Group: 20 Control Group: 10
INDUCTION PHASE Induction Concentration:
intradermal: 5% v/v in arachis oil
topical: 100%
Signs of Irritation Discreet or patchy to moderate and confluent erythema with or without very slight oedema was noted at the topical induction sites of all test group animals at the 1-hour observation and 17 test group animals at the 24-hour observation.
CHALLENGE PHASE Induction Concentration:
topical: 50% and 75% in arachis oil BP
Remarks - Method No significant protocol deviations.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: challenge*

		24 h	*48 h*
Test Group	75%	0	0
	50%	0	0
Control Group	75%	0	0
	50%	0	0

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

TEST FACILITY SafePharm (2000a)

B.5. Skin sensitisation – human volunteers

TEST SUBSTANCE Notified chemical (30% in vehicle)

METHOD Repeated insult patch test with challenge

Study Design Induction Procedure: Patches containing 0.3 mL test substance were applied over 3 weeks for a total of 9 applications. Patches were removed by the applicants after 24 h and graded after an additional 24 h (or ~ 48 h followed the weekend patch removals).
Rest Period: ~2 weeks
Challenge Procedure:

Study Group 6 F, 6 M; age range 21-62 years

Vehicle 75% diethyl phthalate/25% ethanol

Remarks - Method Occluded. The test substance was spread on a 25 mm Hill Top Chamber System using a syringe.

RESULTS

Remarks - Results All 12/12 subjects completed the study. No serious adverse events related to the test substance occurred. During induction faint minimal erythema was seen in two subjects on one day each. During the challenge faint minimal erythema was also seen in two subjects.

CONCLUSION The test substance was non-sensitising under the conditions of the test.

TEST FACILITY HRL (2011)

B.6. 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 S9 preparation

Concentration Range in Main Test a) With metabolic activation: 0 - 5000 µg/plate
b) Without metabolic activation: 0 - 5000 µg/plate

Vehicle Dimethyl sulfoxide

Remarks - Method A preliminary toxicity test (0-5000 µg/plate) was performed to determine the toxicity of the test substance (TA100 or WP2uvrA).

In the mutation studies, aliquots of 0.1 mL of either test substance , negative control solution or positive control solution was used at concentrations up to 5000 µg/plate. In Experiemnt1, WP2uvrA was not tested at 15 µg/plate and in Experiment 2 TA1537, TA98 and WP2uvrA were not tested at 15 µg/plate. The negative control was Dimethyl sulfoxide and positive controls were N-ethyl-N'-nitro-N-nitrosoguanidine, 9-aminoacridine, and 4-nitroquinoline-1-oxide in the absence of S9 mix and 2-aminoanthracene and benzo[a]pyrene in the presence of S9 mix

RESULTS

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

Remarks - Results

The test substance caused a visible reduction in the growth of the bacterial lawn to all of the bacterial tester strains without metabolic activation and TA1535, TA1537 and TA100 with metabolic activation. The test substance was tested up to 5000 µg/plate.

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

All the positive control chemicals used in the test induced marked increases in the frequency of revertant colonies thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.

CONCLUSION

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

TEST FACILITY

SafePharm (2000b)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

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

RESULTS

Notified chemical		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
6	16	6	67
9	15	9	68
15	12	15	63
21	12	21	64
28	15	28	65

Remarks - Results	The validity criteria were achieved after 14 days for the reference substance (sodium benzoate) as degradation exceeded the pass level of 60%. Examination of the degradation curve for the toxicity control showed that the toxicity control attained in excess of 27% degradation by day 14 of the study thereby confirming that the notified chemical was not toxic to the sewage treatment micro-organisms used in the study. The notified chemical attained 15% degradation after 28 days. Therefore, the notified chemical cannot be considered as readily biodegradable under the conditions of OECD Guideline 301D.
CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	Safepharm (2004d)

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