File No: LTD/1865

July 2016

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Vetyvalone

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.

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

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

Director
NICNAS

TABLE OF CONTENTS

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/1865	Firmenich Pty Limited	Vetyvalone	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 of 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*
Acute Toxicity (Category 4) (by inhalation route)	H332 – Harmful if inhaled
Skin Irritation (Category 2)	H315 – Causes skin irritation
Skin Sensitisation (Category 1)	H317 – May cause an allergic skin reaction

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

R20: Harmful by inhalation
R38: Irritating to skin
R43: May cause sensitisation by skin contact

The environmental hazard classification according to the *Globally Harmonised System of 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 2	H401 – Toxic to aquatic life
Chronic Category 2	H411 – Toxic to aquatic life with long lasting effects

Human health risk assessment
Provided that the recommended controls are being adhered to, under the conditions of the occupational settings, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

Based on the information available, when used at ≤ 5% in air fresheners, ≤ 1.3% in fine fragrances and ≤ 0.5% in other cosmetic and 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 and the reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling
- The notified chemical should be classified as follows:
  - Acute Toxicity (Category 4) (by inhalation route): H332 – Harmful if inhaled
  - Skin Irritation (Category 2): H315 – Causes skin irritation

- Skin Sensitisation (Category 1): H317 – May cause an allergic skin reaction

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

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

Health Surveillance

- As the notified chemical is a skin sensitiser, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of sensitisation.

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 processes:
  - 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 processes:
  - Avoid contact with skin and eyes
  - Avoid inhalation of aerosols or mist

- 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:
  - Impervious gloves, eye protection, coveralls
  - Respiratory protection in case of poor ventilation

  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.

Public Health

- The following measures should be taken to minimise public exposure to the notified chemical:
  - The notified chemical should only be used at ≤ 5% in air fresheners, ≤ 1.3% in fine fragrances and 0.5% in other cosmetic products and house hold 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 5% in air fresheners, 1.3% in fine fragrances and 0.5% in other cosmetic and household products

or

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

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

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME
Vetyvalone

MOLECULAR WEIGHT
< 500 Da

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

3. COMPOSITION

DEGREE OF PURITY
> 90 %

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: pale yellow / colourless liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -20 °C	Measured
Boiling Point	272 °C at 98.2 kPa	Measured
Relative Density	0.967 at 20 °C	Measured
Vapour Pressure	1.7×10^{-3} kPa at 25 °C 9.8×10^{-4} kPa at 20 °C	Measured
Water Solubility	0.0247 – 0.112 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Stable	Measured[1]
Partition Coefficient (n-octanol/water)	log Pow = 3.63 – 4.29 at 25 °C[2] log Pow = 4.51 – 4.85 at 30 °C[3]	Measured
Adsorption/Desorption	log K_{oc} = 3.03 – 3.06 at 20 °C	Measured
Dissociation Constant	Not determined	Contains no dissociable functionalities
Flash Point	124 ± 2 °C at 98.2 kPa	Measured
Flammability limits	Not determined	-

Autoignition Temperature	255 °C	Measured
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties

[1] In house method; full study report not provided.
[2] Test conducted using slow-stir method
[3] Test conducted using HPLC method

DISCUSSION OF PROPERTIES
The result obtained using slow-stir method is considered more accurate than result obtained using HPLC method due to the limitations of the HPLC method, which is dependent on reference substances. Hence the result obtained using slow-stir method is used in risk assessment. 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 of 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 not be manufactured in Australia. It will be imported into Australia in the following forms: as the pure chemical to be blended into fragrance formulations or end-use products, as a component of fragrance formulations to be blended into end-use products, or as a component of end-use 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 will be imported in to Australia in lacquered drums of varying sizes ranging from 5 kg to 180 kg. The notified chemical will be transported to warehouse and/or customer reformulation sites by road. After reformulation, the end-use products will be packaged in a variety of container types and sizes depending on the product type and transported by road to retail outlets for sale to public.

USE
The notified chemical will be used as a fragrance ingredient in a wide variety of cosmetic and household products. The content in the final consumer products will vary, with the following proposed usage concentrations: ≤ 5% in air fresheners, ≤ 1.3% in fine fragrances and ≤ 0.5% in other cosmetic and household products.

OPERATION DESCRIPTION
The notified chemical will not be manufactured within Australia. It will be imported into Australia as pure chemical, fragrance ingredient or as a component of end-use products.

Reformulation
The notified chemical will be formulated into fragranced end-use products. In some cases the chemical will first be formulated into a fragrance blend. The procedures for incorporating the notified chemical into blends or end-

use products will likely vary depending on the nature of the cosmetic and household products and may involve both automated and manual transfer steps. However, in general, it is expected that the reformulation process 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.

End-use
The finished products containing the notified chemical may be used by consumers and by professionals such as hairdressers, workers in beauty salons or cleaners. Depending on the type of product, cosmetic products may be applied by hand, spraying or through an applicator and household products may be applied by hand, brush, spraying and dipping. The household products may be further diluted in water before application.

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
Professional end users	Unspecified	Unspecified

EXPOSURE DETAILS

Transport and Storage
Transport and storage workers may come in to contact with the notified chemical at ≤ 100% concentration when handling the imported pure chemical, fragrance formulations and/or end-use products in the event of a spill or rupture of container. The primary work activity undertaken by the workers will be loading and off-loading of containers. Incidental exposure to the notified chemical may occur via skin or eye during the clean-up of accidental spills.

Reformulation
The notified chemical will not be reformulated by the notifier. Reformulation of the notified chemical into fragrance formulation and/or end-use products will be carried out at the facilities of the notifier's customers. During reformulation, dermal, ocular and perhaps inhalation exposure of workers may occur during weighing and transfer stages, blending, quality control analysis, packaging and cleaning and maintenance of equipment. The notifier stated that blending is expected to be carried out using automated equipment, but may contain manual transfer steps.

End-use by professionals
The notified chemical will be used as a fragrance ingredient in cosmetic and household products. Beauty care and cleaning professionals may come into contact with the notified chemical during the use of the products containing the notified chemical. The majority of the products used by these professionals will contain the notified chemical at concentrations ≤ 0.5%. The principal route of exposure will be dermal, ocular and possibly inhalation exposure (from the use spray-on products).

6.1.2. Public Exposure

There will be widespread and repeated exposure of the public to the notified chemical through the use of the cosmetic and household products with ≤ 0.5% concentration of the notified chemical in all the products except air fresheners (≤ 5% concentration) and fine fragrance (≤ 1.3% concentration). The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray.

A combined internal dose of 1.2943 mg/kg bw/day was estimated using data on typical use patterns of cosmetic and household cleaning product categories in which the notified chemical may be used (SCCS, 2012; Cadby *et al.*, 2002; Loretz *et. al.*, 2006; ACI, 2010; specific use details of the notified chemical are considered as exempt information). This estimation assumed a worst case scenario and is for a person who is a simultaneous user of a selection of cosmetic and household products that may contain the notified chemical.

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	LD_{50} > 2,000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD_{50} > 2,000 mg/kg bw; low toxicity
Rat, acute inhalation toxicity	LC_{50} 1.0 – 5.0 mg/L/4 hour; harmful
Rabbit, skin irritation	irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay (LLNA)	evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days.	NOAEL 300 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration test	non genotoxic

Toxicokinetics, metabolism and distribution.
No studies on toxicokinetics, metabolism and distribution were provided. Based on the water solubility (0.0247 – 0.112 g/L at 20 °C), partition coefficient (log P_{ow} 3.63 – 4.29 at 25 °C) and the low molecular weight (< 500 Da) of the notified chemical, passive diffusion across the gastrointestinal tract and dermal absorption is possible. The notified chemical may also be absorbed across the respiratory tract.

Acute toxicity.
The notified chemical was found to be of low toxicity via the oral and dermal routes.

Acute inhalation study conducted on the notified chemical showed that the chemical is harmful via inhalation. All the test animals exposed to 5.1 mg/L of test substance for 4 hours showed signs of toxicity and 3 animals out of six had to be sacrificed on day 3 for ethical reasons. No mortalities and/or signs of toxicity were observed in animals exposed at 1 mg/L of test substance for 4 hours. Thus the LC50 was reported to be between 1.0 and 5.0 mg/L/4 hours.

Irritation and sensitisation.
In a dermal irritation study in rabbits, a single 4-hour, semi-occluded application of the notified chemical resulted in severe erythema and oedema in the treated skin areas of all test animals, which remained until the end of the study. Scaly and/or bald skin was noted in all animals 7 days after exposure, which persisted till the end of the study. The notified chemical was found to be slightly irritating in an acute ocular irritation study conducted on rabbits.

The notified chemical was a skin sensitiser in mice (LLNA). When tested at 25, 50 and 100% concentration, the stimulation indices obtained were 1.9, 2.6 and 4.5. The EC3 value was calculated to be 60.5%.

Repeated dose toxicity.
In a 28 day repeated dose toxicity study by oral gavage, rats were administered the notified chemical at 100, 300 and 1,000 mg/kg bw/day. The No Observed Adverse Effect Level (NOAEL) was established as 300 mg/kg bw/day in this study, based on the changes observed at 1,000 mg/kg bw/day. At this dose liver effects were associated with biochemical changes. Villous hypertrophy of the colon epithelium and indications of extramedullary haematopoiesis were also seen. Lesser effects seen at 300 mg/kg bw/day were considered adaptive.

Mutagenicity/Genotoxicity.
The notified chemical was not mutagenic in a bacterial reverse mutation study and non-clastogenic in an in vitro mammalian chromosome aberration test.

Health hazard classification
Based on the available information, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System of 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*
Acute Toxicity (Category 4) (by inhalation route)	H332 – Harmful if inhaled
Skin Irritation (Category 2)	H315 – Causes skin irritation
Skin Sensitisation (Category 1)	H317 – May cause an allergic skin reaction

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

R20: Harmful by inhalation
R38: Irritating to skin
R43: May cause sensitisation by skin contact

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Reformulation
Exposure of workers to the notified chemical at ≤ 100% concentration may occur during blending operations, quality testing and equipment cleaning and maintenance. The notified chemical has the potential to cause skin irritation and is considered to be a skin sensitiser. In addition, harmful effects following inhalation and/or repeated exposure to the notified chemical is possible. Therefore, caution should be exercised when handling the notified chemical during reformulation process.

Provided that control measures are in place to minimise worker exposure, including the use of automated processes and personal protective equipment (PPE) such as impervious gloves, coveralls, safety glasses and respiratory equipment with gas filter (in cases where there is inadequate ventilation) the risk to the health of workers during the handling of the notified chemical is not considered to be unreasonable.

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

6.3.2. Public Health
Members of the public may experience repeated exposure to the notified chemical through the use of the cosmetic and household products containing the notified chemical at up to 5% concentrations.

Acute toxicity and irritation
The notified chemical has the potential to cause irritation to skin and is harmful if inhaled. However, these effects are not expected from the use of products containing the notified chemical at proposed concentrations in cosmetic and household products.

Repeated dose toxicity
The repeated dose toxicity potential of the notified chemical was estimated by calculation of the margin of exposure (MoE) using the worst case exposure scenario from use of multiple products of 1.2943 mg/kg bw/day (see section 6.1.2) and the NOAEL of 300 mg/kg bw/day, which was established by the study authors in a 28-day repeated dose toxicity study on the notified chemical. A MoE value ≥ 100 is considered acceptable to account for intra- and inter-species differences. Using the above mentioned NOAEL, a MoE of 232 was estimated, which is considered to be acceptable.

Sensitisation
The notified chemical is a weak sensitiser and hence has the potential to cause sensitisation via dermal route upon repeated exposure. Proposed methods for the quantitative risk assessment of dermal sensitisation have been the subject of significant discussion (see for example, Api *et al.*, 2008 and RIVM, 2010). Based on the proposed use concentration and the type of products, a Consumer Exposure Level (CEL) was estimated (SCCS, 2012 and Cadby *et al.*, 2002). An Acceptable Exposure Level (AEL) was also determined using the EC3 value (60.5%) obtained from the LLNA study on the notified chemical. In this instance, the factors employed included an interspecies factor (3), intraspecies factor (10), a matrix factor (3.16) and a use and time factor (3.16), giving an overall safety factor of ~300. The CEL was less than the AEL for all products, using the proposed concentrations of the notified chemical.

Based on the lower expected exposure level from use of household products (≤ 0.5% notified chemical), by inference, the risk of induction of sensitisation associated with the use of these products is also not considered to be unreasonable. It is acknowledged that consumers may be exposed to multiple products containing the notified chemical, and a quantitative assessment based on the aggregate exposure has not been conducted.

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at ≤ 5.0% in air fresheners, ≤ 1.3% in fine fragrances and ≤ 0.5% in other cosmetic and household 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 raw material or as a component of fragrance preparations, for local reformulation into a variety of end-use consumer products (cosmetic and household products). The notified chemical will also be imported as a component of finished consumer products. Release during reformulation in Australia is expected to be limited to accidental spills or leaks of drums (0.1%) and residue in import containers (< 0.1%). Waste water from reformulation equipment cleaning is expected to be discharged to an on-site and/or local wastewater treatment plant for recycling. Therefore, a total of < 0.2%, or 2 kg of the import volume, is estimated to be released from reformulation in Australia.

RELEASE OF CHEMICAL FROM USE
The notified chemical is expected to be released to the aquatic compartment through sewers during its use in various cosmetic and domestic end-products.

RELEASE OF CHEMICAL FROM DISPOSAL
It is estimated that a maximum of 3% or up to 30 kg of the notified chemical may remain in end-use containers once the consumer products are used up. These will be disposed of through domestic garbage disposal to landfill or recycled through an approved waste management facility.

7.1.2. Environmental Fate
Following its use in Australia, the majority of the notified chemical is expected to enter the sewer system through its use as a component of cosmetic and household products, before potential release to surface waters nationwide. The notified chemical is not considered readily biodegradable (3% in 28 days), but shows ultimate biodegradability (64% in 100 days). For details of the environmental fate study, please refer to Appendix C. Based on its measured adsorption coefficient (log K_{OC} = 3.03-3.06), release to surface waters may occur, as only partial partitioning to sludge is expected. The notified chemical has the potential to bioaccumulate due to its n-octanol/water partition coefficient (log P_{OW} = 3.63-4.29 at 25 °C) and lack of ready biodegradability. However, bioaccumulation is not expected to occur as the notified chemical is not expected to be present in ecotoxicologically significant concentrations, due to its moderate volatility, potential to adsorb to soil and sediment, and ultimate biodegradability. In surface waters, the notified chemical is expected to eventually disperse and degrade through biotic and abiotic processes to form water and oxides of carbon.

Based on its vapour pressure (9.8×10^{-4} kPa), the notified chemical is moderately volatile from water and may slowly volatilise to air during use and in sewage treatment. The half-life of the notified chemical in air is

calculated to be 3.411 h, based on reactions with hydroxyl radicals (AOPWIN v1.92; US EPA, 2011). Therefore, the notified chemical is not expected to persist in the air compartment.

The majority of the notified chemical will be released to sewer after use. A small proportion of the 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 as collected spills and empty containers. The notified chemical in landfill, soil and sludge is expected to have limited mobility based on the reported adsorption coefficient (log K_{OC} = 3.03-3.06), and is expected to eventually degrade to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated to assume a worst case scenario, with 100% release of the notified chemical into sewer systems nationwide and no removal within sewage treatment plants (STPs).

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:	0.606	µg/L
PEC - Ocean:	0.061	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 the notified chemical in the applied soil in 5 and 10 years may be approximately 20.19 µg/kg and 40.39 µg/kg, respectively.

7.2. Environmental Effects Assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h LC50 = 4.254 mg/L	Toxic to fish
Daphnia Toxicity	48 h EL50 = 4.3 mg/L*	Toxic to *Daphnia*
Algal Toxicity	72 h E_rL50 = 5.164 mg/L*	Toxic to algae
	72 h E_bL50 = 0.687 mg/L*	
Inhibition of Bacterial Respiration	3 h IC50 ≈1000 mg/L	Not inhibitory to bacterial respiration

* Water Accommodated Fraction

Based on the above acute ecotoxicological endpoints, the notified chemical is expected to be toxic to aquatic life. Therefore, under the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)* (United Nations, 2009), the notified chemical is formally classified as "Acute Category 2; Toxic to aquatic life". Based on its acute toxicity and lack of ready biodegradability, under the GHS the notified chemical is formally classified 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 most sensitive endpoint for fish. A safety factor of 100 was used given acute endpoints for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LC50 (Fish, 96 h)	4.254	mg/L
Assessment Factor	100	
Mitigation Factor	1.00	
PNEC:	42.54	µg/L

7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) has been calculated based on the predicted PEC and PNEC.

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.606	42.54	**0.014**
Q - Ocean	0.061	42.54	**0.001**

The risk quotient for discharge of treated effluents containing the notified chemical to the aquatic environment indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in surface waters based on its maximum annual importation quantity. Whilst the notified chemical is not readily biodegradable, it is considered ultimately biodegradable and is not expected to bioaccumulate. On the basis of the PEC/PNEC ratio, maximum annual importation volume and assessed use pattern in cosmetic and household products, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point < -20 °C

Method	OECD TG 102 Melting Point/Melting Range.
Remarks	BS4633 method for determination of crystallizing point. The data is derived from two independent determinations.
Test Facility	Firmenich (2013a)

Boiling Point 272 ± 2 °C at 98.2 kPa

Method	OECD TG 103 Boiling Point.
Remarks	Siwoloboff method. The data is derived from three independent determinations.
Test Facility	Firmenich (2013a)

Relative Density 0.967 at 20 °C

Method	OECD TG 109 Density of Liquids and Solids.
Remarks	Oscillating density meter method. The data is derived from three independent determinations.
Test Facility	Firmenich (2013a)

Vapour Pressure 1.7×10^{-3} kPa at 25 °C
9.8×10^{-4} kPa at 20 °C

Method	OECD TG 104 Vapour Pressure.
Remarks	Isothermal thermogravimetric effusion method.
Test Facility	WIL (2014a)

Water Solubility 0.112 g/L at 20 °C

Method	OECD TG 105 Water Solubility. EC Council Regulation No 440/2008 A.6 Water Solubility.
Remarks	Flask Method
Test Facility	Firmenich (2013a)

Water Solubility 0.0247 g/L at 20 °C

Method	OECD TG 105 Water Solubility. EC Council Regulation No 440/2008 A.6 Water Solubility.
Remarks	Column Elution Method
Test Facility	WIL (2014b)

Partition Coefficient (n-octanol/water) log Pow = 4.51-4.85 at 30 °C

Method	OECD TG 117 Partition Coefficient (n-octanol/water). EC Council Regulation No 440/2008 A.8 Partition Coefficient.
Remarks	HPLC Method
Test Facility	Firmenich (2013a)

Partition Coefficient (n-octanol/water) log Pow = 3.63-4.29 at 25 °C

Method	OECD TG 123 Partition Coefficient (n-octanol/water).
Remarks	Slow-stir Method
Test Facility	Harlan (2014)

Adsorption/Desorption log K_{oc} = 3.03-3.06 at 20 °C

Method	OECD TG 106 Adsorption - Desorption Using a Batch Equilibrium Method.
Remarks	Adsorption parameters were determined in three different soil types.
Test Facility	WIL (2014c)

Flash Point 124 ± 2 °C at 98.2 kPa

Method	EC Council Regulation No 440/2008 A.9 Flash Point.
Remarks	Closed cup equilibrium method. The data is derived from two independent determinations following a preliminary test.
Test Facility	Firmenich (2013a)

Autoignition Temperature 255 °C

Method	EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks	Atmospheric pressure was between 99.75 – 100.29 kPa. The result was based on the minimum autoignition temperature observed, rounded down to the nearest 5ºC.
Test Facility	WIL (2014a)

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 Wistar/Crl:WI (Han)
- Vehicle: None
- Remarks - Method: No significant deviations from the OECD guidelines.

RESULTS

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

- LD50: > 2,000 mg/kg bw
- Signs of Toxicity: One animal from group 2 in moribund condition was sacrificed on day 2 for humane reasons. The animal showed lethargy, hunched posture, uncoordinated movements, slow breathing, piloerection, salivation, ptosis, hypothermia and yellow urine.

  Clinical signs noted among surviving animals between day 1 and 4 included lethargy, hunched posture, uncoordinated movement, slow breathing, shallow respiration, piloerection, salivation, watery discharge for both eyes, and/or hypothermia. These signs were not observed in any of the surviving animals from day 5.
- Effects in Organs: None reported
- Remarks - Results: All the surviving test animals gained weight over the course of the study. Based on the results, the LD50 of the notified chemical is estimated to be > 2,000 mg/kg bw.

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

TEST FACILITY: WIL (2014d)

B.2. Acute toxicity – dermal

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 402 Acute Dermal Toxicity – Limit Test.
- Species/Strain: Rat/Crl:WI (Han)
- Vehicle: None
- Type of dressing: Occlusive
- Remarks - Method: No significant deviations from the OECD guidelines.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 F & 5 M	2,000	0/10

- LD50: > 2,000 mg/kg bw
- Signs of Toxicity - Local: Swelling, general erythema and/or dryness were noted on the treated skin area of all animals between days 2 and 6. Scales were noted on the treated skin of several animals between days 7 and 13.
- Signs of Toxicity - Systemic: Lethargy, hunched posture, piloerection, chromodacryorrhoea and/or

	ptosis were noted in all animals after dosing, and were resolved in all animals by day 9. Body weight gain was as expected.
Effects in Organs	Pelvic dilation in the right kidney of one animal was not considered to be treatment related.
Remarks - Results	The study authors commented that some of the clinical signs may be related to the local skin effects rather than direct toxicity. The LD50 was estimated to be > 2,000 mg/kg bw.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	WIL (2014e)

B.3. Acute toxicity – inhalation

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 436 Acute Inhalation Toxicity – Acute Toxic Class Method.
Species/Strain	Rat/Crl:WI (Han)
Vehicle	None
Method of Exposure	Oro-nasal exposure.
Exposure Period	4 hours
Physical Form	solid aerosol (particulate).
Particle Size	3.7 - 4.0 μm (MMAD)
Remarks - Method	No significant deviations from the OECD guidelines. The Mass Median Aerodynamic Diameter (MMAD) of the particles was in the range 3.7 to 4.3μm.

RESULTS

Group	*Number and Sex of Animals*	*Concentration mg/L*		*Mortality*
		Nominal	*Actual*	
1	3 F & 3 M	8.0	5.1 ± 0.1	1/3 (M) & 2/3 (F)
2	3 F & 3 M	1.89	1.0 ± 0.03	0/6

LC50	1.0 – 5.0 mg/L/ 4 hours
Signs of Toxicity	In group 1, all animals showed slow breathing during exposure. After exposure, lethargy, hunched posture, flat posture, uncoordinated movements, laboured respiration, ptosis, rales and/or hypothermia were seen among the animals. One male and two female rats were sacrificed for ethical reasons on day 3. The remaining surviving animals had recovered from the symptoms between days 5 and 6. No mortality and/or clinical signs of systemic toxicity were noted in group 2 animals. Body weights decreased during the first two days after treatment in group one animals and in group 2 males and was static in group 2 females. Weight gains were seen in all animals after this.
Effects in Organs	Gelatinous content of the stomach and/or duodenum were seen in the two Group 1 females that were sacrificed for ethical reasons. No other treatment-related effects were seen at necropsy. Pelvic dilation of the right kidney in one Group 1 female was not considered to be related to treatment.
Remarks - Results	The LC50 was considered to be within the range of 1.0 to 5.0 mg/L.
CONCLUSION	The notified chemical is harmful via inhalation.
TEST FACILITY	WIL (2014f)

B.4. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3M
Vehicle	None
Observation Period	14 days
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant deviations from the OECD guidelines. 0.5 ml of test substance was applied on 2×3 cm patch and kept in contact with the clipped skin for 4 hours.

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	2.0	2.7	2.7	3	14 days	2
Oedema	4.0	3.0	3.3	4	14 days	1

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

Remarks - Results

Four hour exposure to test substance resulted in moderate to severe erythema and oedema in the treated skin areas of the three rabbits, which remained until study termination (14 days). Reduced flexibility of the skin was noted for one animal at 72 hours and 7 days post exposure. Scaliness and/or bald skin were noted for all animals 7 days after exposure and persisted until termination. No signs of systemic toxicity were observed during the course of the study.

Although bald skin (which can be an outcome of corrosion) was noted at the end of the observation period, the study authors stated that no evidence of full thickness destruction of the skin or scar tissue was observed during the duration of the study, and therefore they considered that the test substance was not corrosive.

CONCLUSION	The notified chemical is irritating to the skin.
TEST FACILITY	WIL (2014g)

B.5. Irritation – eye

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion (2012).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3M
Observation Period	72 hours
Remarks - Method	No significant deviations from the OECD guidelines.

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	0.7	0.3	2	< 72 h	0
Conjunctiva: chemosis	0.0	0.0	0.0	1	< 24 h	0
Conjunctiva: discharge	0.0	0.0	0.0	2	< 24 h	0

Corneal opacity	0.0	0.0	0.0	0	-	0
Iridial inflammation	0.0	0.0	0.0	0	-	0

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

Remarks - Results: Treatment of the eyes with 2% fluorescein 24 hours after test substance instillation revealed no corneal epithelial damage.

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

TEST FACILITY: WIL (2014h)

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

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 429 Skin Sensitisation: Local Lymph Node Assay (2010)

Species/Strain: Mouse/CBA/J

Vehicle: Acetone/Olive oil mixture (4:1 v/v)

Preliminary study: Yes

Positive control: Not conducted in parallel with the test substance, but had been conducted previously in the test laboratory using α-hexylcinnamaldehyde.

Remarks - Method: A preliminary study was conducted to determine the highest test substance concentration to be used in the main study, in order to rule out excessive irritation and systemic toxicity.

RESULTS

Concentration (% w/w)	*Number and sex of animals*	*Proliferative response (DPM ± SEM)*	*Stimulation Index (Test/Control Ratio)*
Test Substance			
0 (vehicle control)	5 F	240 ± 36	-
25	5 F	444 ± 36	1.9
50	5 F	629 ± 92	2.6
100	5 F	1089 ± 130	4.5

EC3: 60.5%

Remarks - Results: In the main study at 50% test substance concentration, very slight erythema was noted for all animals on both ears between day 2 and 5 and for 4 animals on day 6. At a 100% concentration, erythema was noted on both ears for all animals and scales were noted on both ears of all animals on day 6. No clinical signs of systemic toxicity were observed in any of the treated animals.

A dose-related increase in stimulation index was found for the notified chemical, which exceeded 3 at the highest concentration tested.
The non-concurrent test on the positive control α-hexylcinnamaldehyde showed a dose-related increase in the stimulation index, confirming the validity of the test system.

CONCLUSION: There was evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.

TEST FACILITY: WIL (2014i)

B.7. Repeat dose toxicity

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.

Species/Strain: Rat: Crl:WI(Han)

Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week
Vehicle	Polyethylene glycol 400
Remarks - Method	No significant deviations from the OECD guideline.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5F & 5M	0	0
low dose	5F & 5M	100	0
mid dose	5F & 5M	300	0
high dose	5F & 5M	1,000	0

Mortality and Time to Death
All the animals survived the study duration.

Clinical Observations
Salivation after dosing was observed in all animals from the mid and high groups and in females from the low dose group. This was considered to be a physiological response rather than a sign of systemic toxicity, considering the mild nature and its time of occurrence. No other clinical signs of toxicity and/or functional abnormalities were noted during the course of the study.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Male rats from the high dose group showed low blood cell counts, haemoglobin and haematocrit values, and higher reticulocyte counts, red cell distribution width and mean corpuscular haemoglobin concentration. Similarly female rats from the high dose group showed higher reticulocyte counts when compared to controls.

The following clinical observations were noted (compared to controls):
- higher total protein and cholesterol levels in female rats from high dose group
- higher total bilirubin level in rats from high and mid dose groups
- higher creatinine and lower glucose levels in all male rats exposed to the test substance
- higher inorganic phosphate level in males from the high dose group
- lower chloride level in rats from the high dose group

Two female rats from the high dose group also had higher alanine aminotransferase and aspartate aminotransferase activity when compared to control.

With the exception of higher total bilirubin level at high dose, all the above changes either remained within or marginally exceeded the range of values considered normal for rats of this age and strain.

Two control female rats showed decreased lymphocyte counts but no apparent cause was found.

Effects in Organs
A significant dose-related increase in absolute and relative liver weights was observed in rats from the high and mid dose groups. The relative increase was 37 and 10% in males and 57 and 24% in females for the high and mid doses respectively. An accentuated lobular pattern of the liver was observed in 2 male and 2 female high dose animals and in 1 male from the mid dose group. Increase in liver size was also noted in animals from the high dose group.

Greenish discoloration of both kidneys was observed in 3 male rats from the high dose and 1 male rat from the mid dose group. The absolute and relative weights of kidneys were also increased in rats from high dose group (approximately 20% relative increase in weight).

A significant increase in spleen size and weight was observed in male rats from the high dose group, with the relative spleen weights increased by approximately 28%.

The above changes were reflected in histopathological studies of the organs. In particular, some animals from the high dose group showed minimal coagulative necrosis in the liver. The high dose group also showed an

increase in incidence and severity of hepatocellular vacuolation and hepatocellular hypertrophy, compared to the controls and lower dose groups. Other effects observed in the high dose group were erythroid hyperplasia of bone marrow in 3 males and 4 female rats, and hypertrophy of the villous epithelium in 4 males.

An increase in the severity of cortical hyaline droplets in the kidneys of treated males was not accompanied by tubular or other renal damage, and was thus attributed to the effects of alpha-2 microglobulin, which is species and sex specific.

Remarks – Results
Although some changes were observed in animals from mid dose group including increase in liver weight, there was no evidence of irreversible changes such as microscopic cellular death. The changes at this dosage were considered adaptive in nature and not toxicologically significant.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 300 mg/kg bw/day in this study, based on the toxicologically significant clinical and histopathological changes observed in the high dose group animals.

TEST FACILITY WIL (2014j)

B.8. 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 fraction from phenobarbitone/β-naphthoflavone-induced rat liver (5% in Tests 1 and 3, and 10% in Test 2).
Concentration Range in Main Test	a) With metabolic activation: 1 – 5,000 µg/plate b) Without metabolic activation: 1 – 5,000 µg/plate
Vehicle	Dimethyl sulfoxide
Remarks - Method	No significant deviations from the OECD guidelines. A preliminary test (3 – 5,000 µg/plate; plate incorporation) was performed for strains TA100 and WP2uvrA (with and without S9-mix) to determine the toxicity of the test material. Bacterial strain specific cytotoxicity was observed. No precipitation was observed up to the highest tested dose of 5,000 µg/plate. With the addition of the other three strains, the preliminary test was used as the basis of Test 1. A third test was performed on TA98 with 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	≥ 333	≥ 333	> 5,000	Negative
Test 2		≥ 333	> 5,000	Negative
Present				
Test 1	≥ 333	≥ 333	> 5,000	Negative
Test 2		≥ 333	≥ 5,000	Negative
Test 3		≥ 333	≥ 5,000	Negative

Remarks - Results
Visible reduction in the growth of the bacterial background lawn was seen in all tester strains, with and without metabolic activation.

No increases in the frequency of revertant colonies were recorded for any of the bacterial strains.

The positive controls produced satisfactory responses, 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 WIL (2013)

B.9. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical

METHOD OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Species/Strain Human
Cell Type/Cell Line Lymphocytes/peripheral
Metabolic Activation System S9 fraction from phenobarbitone/β-naphthoflavone-induced rat liver
Vehicle Dimethyl sulfoxide
Remarks - Method No significant deviations from the OECD guidelines.

A preliminary range finding study was conducted to measure the solubility and cytotoxic effects of test substance.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	1*, 10*, 100, 120*, 140 and 160	3 h	24 h
Test 2	3, 10, 30, 50*, 75* and 100*	24 h	24 h
	3*, 10, 30*, 50, 75* and 100	48 h	48 h
Present			
Test 1	1*, 10, 100*, 120, 140* and 160	3 h	24 h
Test 2	3, 10, 30, 50*, 100*, 150* and 200	3 h	48 h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*		
	Cytotoxicity	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	≥ 120	≥ 160	Negative
Test 2 (24 h)	≥ 100	> 100	Negative
Test 2 (48 h)	≥ 75	> 100	Negative
Present			
Test 1	≥ 160	≥ 160	Negative
Test 2	> 150	≥ 200	Negative

Remarks - Results No statistically significant increase in the frequency of cells with chromosomal aberrations, polyploid cells or cells with endoreduplicated chromosomes was seen at any dose levels, with and without metabolic activation.

The positive and negative controls produced satisfactory responses confirming the validity of the test system.

CONCLUSION The notified chemical was not clastogenic to human lymphocytes treated *in vitro* under the conditions of the test.

TEST FACILITY WIL (2014k)

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	River water without particles 3 km downstream from a local domestic wastewater treatment plant.
Exposure Period	28 days (extended to 100 days)
Auxiliary Solvent	None
Analytical Monitoring	Theoretical Oxygen Demand (ThOD)
Remarks - Method	Ammonium chloride was omitted from the test medium to prevent oxygen consumption due to nitrification. Raw river water was used as the inoculums instead of effluent. The exposure duration was extended from 28 days to 100 days due to the long lag phase at the beginning of the test. No other deviation in protocol was reported.

RESULTS

Test substance		*Sodium acetate*	
Day	*% Degradation*	*Day*	*% Degradation*
0	0	0	0
7	0	7	70
14	0	14	73
21	0		
28	3		
42	8		
60	24		
100	64		

Remarks - Results	All validity criteria for the test were satisfied. The percentage degradation of the reference compound reached the threshold level of 60% by 7 days (70%) and attained 83% degradation by 28 days. Therefore, the test indicates the suitability of the inoculums. The test substance attained 3% degradation by 28 days, and a degradation plateau was not achieved. The test was therefore prolonged to 100 days. The test substance attained 64% degradation by 100 days, and a degradation plateau was not achieved. Therefore, the test substance cannot be classified as readily biodegradable according to the OECD (301 D) guideline; however, the test substance exhibited ultimate biodegradability.
CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	Akzo Nobel (2012)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test – Semi-static.
Species	*Brachydanio rerio* (zebra fish)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	45 mg $CaCO_3$/L

Analytical Monitoring	GC
Remarks – Method	The definitive test was conducted at the nominal concentrations of 2.0, 2.5, 3.1, 3.9, and 4.9 mg/L of the test substance. No significant deviations in protocol were reported.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality (%)*				
Nominal	*Actual*		*0 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	Control	7	0	0	0	0	0
2.0	1.86	7	0	0	0	0	0
2.5	2.15	7	0	0	0	0	0
3.1	2.63	7	0	0	0	0	4.76
3.9	4.12	7	0	0	0	4.76	14.3
4.9	4.34	7	0	14.3	61.9	90.5	90.5

LC50	4.25 mg/L (95% CI 4.0-4.53 mg/L) at 96 hours.
NOEC	Not determined.
Remarks – Results	All validity criteria for the test were satisfied. The test solutions were renewed every 24 hours during the 96 h test period. The actual concentrations of the test substance were measured at the start and end of the test period and after every test solution renewal during the 96 h test period. The 96 h LC50 for fish was determined to be 4.25 mg/L, based on nominal concentrations.

CONCLUSION Under the study conditions, the notified chemical is considered to be toxic to fish.

TEST FACILITY Suzhou Research (2013)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – Static.

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	180 mg $CaCO_3$/L
Analytical Monitoring	GC-MS
Remarks - Method	The test substance was prepared as a Water Accommodated Fraction (WAF) due to its low water solubility. Following two days of stirring, a suspension of the test substance was allowed to settle for one hour then filtered to produce a WAF. The definitive test was conducted at the nominal loading rates of 0.46, 1.0, 2.2, 4.6, and 10 mg/L of the test substance. A total of 20 daphnids (5 daphnids/replicate across 4 replicates) were used. No significant deviations in protocol were reported.

RESULTS

Concentration (filtered WAF;mg/L)			*Number of D. magna*	*Cumulative Immobilised (%)*	
Nominal	*Actual*			*24 h*	*48 h*
	0 h	*48 h*			
Control	Control	Control	20	0	0
0.46	0.37	0.287	20	0	0
1.0	1.0	0.748	20	0	0
2.2	1.9	1.42	20	0	0
4.6	4.8	3.74	20	20	45

10.0	10.0	8.15	20	70	100

EL50 4.3 mg/L (WAF) at 48 hours.
NOEL Not determined.
Remarks - Results All validity criteria for the test were satisfied. The test solutions were not renewed during the 48 h test period. The actual concentrations of the test substance in the WAFs were measured at 0 and 48 hours within the 48 h test period. The 48 h EC50 for daphnia was determined to be 4.3 mg/L (WAF), based on measured concentrations.

CONCLUSION Under the study conditions, the notified chemical is considered to be toxic to aquatic invertebrates.

TEST FACILITY WIL (2014l)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE Notified chemical

METHOD OECD TG 201 Alga, Growth Inhibition Test.
Species *Pseudokirchneriella subcapitata* (green alga)
Exposure Period 72 hours
Concentration Range Nominal: 1-100 mg/L
Actual: 0.088-7.0 mg/L (time weighted average)
Auxiliary Solvent None
Water Hardness 24 mg $CaCO_3$/L
Analytical Monitoring GC-MS
Remarks - Method The test substance was prepared as a Water Accommodated Fraction (WAF) due to its low water solubility. Following two days of stirring, a suspension of the test substance was allowed to settle for one hour then filtered to produce a WAF. The definitive test was conducted at the nominal loading rates of 1, 3.2, 10, 32, and 100 mg/L of the test substance. No significant deviations in protocol were reported.

RESULTS

Biomass		*Growth*	
E_bL50 *mg/L at 72 h*	*NOE_bL* *mg/L*	*E_rL50* *mg/L at 72 h*	*NOE_rL* *mg/L*
0.687	< 0.088	5.164	Not determined

Remarks - Results All validity criteria for the test were satisfied. The actual concentrations of the notified chemical were measured at 0, 24 and 72 hours within the 72 h test period. The 72 h E_bL50 and E_rL50 were determined to be 0.687 mg/L (WAF) and 5.164 mg/L (WAF), respectively, based on measured concentrations. The 72 h NOE_bL was determined to be < 0.088 mg/L (WAF).

CONCLUSION Under the study conditions, the notified chemical is considered to be toxic to algae.

TEST FACILITY WIL (2014m)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE Notified chemical

METHOD OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum Aerated activated sludge.
Exposure Period 3 hours

Concentration Range	Nominal: 10-1000 mg/L Actual: Not determined
Remarks – Method	Chemical 3,5-dichlorophenol was used as the reference control. The respiration rate was determined by measurement of BOD during the test after 3 hours of exposure. No significant deviations in protocol were reported.

RESULTS

IC50	1000 mg/L at 3 hours.
Remarks – Results	All validity criteria for the test were satisfied. At the highest concentration tested, 39-53% inhibition of respiration was observed after 3 hours. The 3 h IC50 was therefore determined to be ~1000 mg/L, based on nominal concentrations.

CONCLUSION	The notified chemical is not inhibitory to microbial activity.
TEST FACILITY	WIL (2014n)

BIBLIOGRAPHY

ACI (2010) Consumer Product Ingredient Safety, Exposure and risk screening methods for consumer product ingredients, 2nd Edition, American Cleaning Institute, Washington DC

Akzo Nobel (2012) [Notified chemical] Biodegradation in an Enhanced Biodegradability Test; Closed Bottle Test Method (OECD TG 301 D) (Study No. T11053 C, March, 2012). Arnhem, The Netherlands, Akzo Nobel NV (Unpublished report submitted by the notifier).

Api AM, Basketter DA, Cadby PA, Cano MF, Ellis G, Gerberick GF, Griem P, McNamee PM, Ryan CA and Safford R (2008) Dermal Sensitisation Quantitative Risk Assessment (QRA) for Fragrance Ingredients, Regulatory Toxicology and Pharmacology, 52:3-23.

Cadby, PA, Troy, WR and Vey, MGH (2002) Consumer Exposure to Fragrance Ingredients: Providing Estimates for Safety Evaluation. Regulatory Toxicology and Pharmacology, 36:246-52.

Firmenich (2013a) [Notified chemical] Determination of General Physico-chemical Properties: Freezing Point, Boiling Temperature, Relative Density, Flash Point, Partition Coefficient and Water Solubility (Study No. E110-08.2013, October, 2013). La Plaine, Switzerland, Firmenich, Laboratory of Analysis and Measurement (Unpublished report submitted by the notifier).

Harlan (2014) [Notified chemical] Determination of Partition Coefficient by the Slow-stir Method (Study No. 41301616, March, 2014). Derby, U.K., Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

Loretz et al. (2006) Loretz, L., Api, A.M., Barraj, L., Burdick, J. Davis, D.A., Dressler, W., Gilberti, E., Jarrett, G., Mann, S., Pan, Y.H.L., Re, T., Renskers, K., Scrafford, C., Vater, S.;Exposure data for personal care products : Hairspray, spray perfume, liquid foundation, shampoo, body wash, and solid antiperspirant, Food and Chemical Toxicology 44 (2006) 2008-2018

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

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

Suzhou Research (2013) [Notified chemical] Acute Toxicity Test on Zebrafish (According to OECD TG 203) (Study No. 2013-036-02-01, October, 2013). Suzhou, China, Suzhou Xisha Zhongke Drug R&D Co. Ltd. (Unpublished report submitted by the notifier).

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

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

WIL (2013) [Notified chemical] Evaluation of The Mutagenic Activity In The *Salmonella typhimurium* Reverse Mutation Assay And The *Escherichia coli* Reverse Mutation Assay (With Independent Repeat) (Study No. 502844, September, 2013). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014a) [Notified chemical] Determination of Physico-Chemical Properties: Vapour Pressure and Auto-ignition Temperature (Study No. 502845, August, 2014). The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014b) [Notified chemical] Determination of the Solubility in Water and in Iso-Medium (Study No. 504944, July, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014c) [Notified chemical] Adsorption on Three Soils (Study No. 502858, July, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014d) [Notified chemical] Assessment of Acute Oral Toxicity In The Rat (Acute Toxic Class Method) (Study No. 502847, July, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014e) [Notified chemical] Assessment of Acute Dermal Toxicity In The Rat (Study No. 502848, July, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014f) [Notified chemical] Assessment of Acute Inhalation Toxicity In The rat (Study No. 502846, January, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014g) [Notified chemical] Primary Skin Irritation/Corrosion Study In The Rabbit (4-Hour Semi-Occlusive Application) (Study No. 502849, July, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014h) [Notified chemical] Acute Eye Irritation/Corrosion Study In The Rabbit (Study No. 502850, July, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014i) [Notified chemical] Assessment of Contact Hypersensitivity In The Mouse (Local Lymph Node Assay) (Study No. 502851, July, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014j) [Notified chemical] Repeated Dose 28-Day Oral Toxicity Study By Daily Gavage In The Rat (Study No. 502853, July, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014k) [Notified chemical] Evaluation of The Ability of The Notified Chemical To Induce Chromosome Aberrations In Cultured Peripheral Human Lymphocytes (With Repeat Experiment) (Study No. 502854, June, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014l) [Notified chemical] Acute Toxicity Study in *Daphnia magna* (Static) (Study No. 502856, November, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014m) [Notified chemical] Fresh Water Algal Growth Inhibition Test (Study No. 502855, November, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2014n) [Notified chemical] Activated Sludge Respiration Inhibition Test (Carbon and Ammonium Oxidation) (Static) (Study No. 502857, May, 2014). Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).