File No: LTD/1544

February 2013

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Walnut Ester

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health and Ageing, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of Sustainability, Environment, Water, Population and Communities.

For the purposes of subsection 78(1) of the Act, this Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

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

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Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS SUBSTANCE	INTRODUCTION VOLUME	USE
LTD/1544	Firmenich Limited	Walnut Ester	Yes	≤1 tonne per annum	Component of cosmetic and household cleaning products

*ND = not determined

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

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

R43: May cause sensitisation by skin contact

The environmental hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals* (GHS) is presented below. Environmental classification under the GHS is not mandated in Australia and carries no legal status but is presented for information purposes.

Hazard classification	*Hazard statement*
Acute Aquatic Toxicity (Category 2)	H401: Toxic to aquatic life
Chronic Aquatic Toxicity (Category 3)	H412: Harmful to aquatic life with long lasting effects

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

When used at ≤0.02% in deodorants, ≤0.04% in fine fragrances, ≤0.06% in other leave-on cosmetic products, ≤0.7% in rinse-off cosmetic products and ≤0.9% in household cleaning 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:
  - Skin sensitisation (Category 1): H317 – May cause an allergic skin reaction

- The following should be used for products/mixtures containing the notified chemical:
  - Conc. ≥1%: H317

- 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 isolation and 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

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical during reformulation processes:
  - Coveralls, impervious gloves

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

- If cleaners and/or beauty care professionals are frequently applying products containing the notified chemical to clients/surfaces, a person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure of workers to the notified chemical:
  - Avoid contact with skin

- If cleaners and/or beauty care professionals are frequently applying products containing the notified chemical to clients/surfaces, 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:
  - Impervious gloves

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

- A copy of the (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 must 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 ≤0.02% in deodorants, ≤0.04% in fine fragrances, ≤0.06% in other leave-on cosmetic products, ≤0.7% in rinse-off cosmetic products and ≤0.9% in household cleaning products.

Disposal

- The notified chemical should be disposed of to landfill.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical/polymer 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 0.02% in deodorants, 0.04% in fine fragrances, 0.06% in other leave-on cosmetic products, 0.7% in rinse-off cosmetic products and 0.9% in household cleaning products;

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of cosmetic and household cleaning products, or is likely to change significantly;
  - the chemical has begun to be manufactured in Australia;
  - additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

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

(Material) Safety Data Sheet
The (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

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

1. APPLICANT AND NOTIFICATION DETAILS

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

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

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

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

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

NOTIFICATION IN OTHER COUNTRIES
USA (2000), EU (2000), Philippines (2002), Switzerland (2002)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Walnut Ester

MOLECULAR WEIGHT
<500 Da

ANALYTICAL DATA
Reference NMR, IR, 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 liquid

Property	Value	Data Source/Justification
Freezing Point	<-81 °C	Measured
Boiling Point	186-187 °C	Measured
Density	967 kg/m^3 at 20 °C	Measured
Vapour Pressure	0.096 kPa at 25 °C	Estimated - mean VP of Antoine & Grain methods (US EPA, 2009)
Water Solubility	4.93 g/L at 21 °C	Measured
Hydrolysis as a Function of pH	$t_{½}$ at 40 °C: 6 days at pH 2 2 days at pH 5	Measured

	<1 day at pH 7 and 8.5 <1 hour at pH 12	
Partition Coefficient (n-octanol/water)	log Pow = 2.5 at 22.5 ºC	Measured
Adsorption/Desorption	log K_{oc} = 0.95	Calculated – EpiSuite v1.66
Dissociation Constant	Not determined	No dissociable functionalities
Flash Point	65 ºC at 101.3 kPa	Measured (closed cup).
Flammability	Not determined	Based on the flash point, not classified as flammable (NTC, 2007)
Autoignition Temperature	>460 ºC	Measured. Full study report in English not provided.
Explosive Properties	Predicted negative	Contains no functional groups that would imply explosive properties.
Oxidative Properties	Predicted negative	Contains no functional groups that would imply oxidative properties.

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

Reactivity
The notified chemical is expected to be stable under normal conditions of use. Temperatures near or above the flash point should be avoided during transport and storage.

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 be imported into Australia as a component (≤25%) of compounded fragrances.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	≤1	≤1	≤1	≤1	≤1

PORT OF ENTRY
Sydney

IDENTITY OF MANUFACTURER/RECIPIENTS
Firmenich Ltd

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

USE
The notified chemical is intended to be used as a component of fragrances for a variety of cosmetic and domestic products (proposed usage concentration: ≤1.15% in fine fragrances, ≤2.5% in other cosmetic products and ≤25% in household cleaning products).

OPERATION DESCRIPTION

The procedures for incorporating the imported products (containing ≤25% notified chemical) into end-use products will likely vary depending on the nature of the cosmetic and household cleaning products formulated, and may involve both automated and manual transfer steps. However, in general, it is expected that the reformulation processes will involve blending operations that will be highly automated and occur in a fully enclosed environment, followed by automated filling of the reformulated products into containers of various sizes.

The finished products containing the notified chemical may be used by consumers and professionals such as hairdressers, workers in beauty salons or cleaners. Depending on the nature of the product, these could be applied in a number of ways, such as by hand, using an applicator or sprayed.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

NUMBER AND CATEGORY OF WORKERS

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

EXPOSURE DETAILS

Transport and storage workers may come into contact with the notified chemical, as a component of the imported products or end-use products (≤25%), only in the event of accidental rupture of containers.

During reformulation, dermal, ocular and perhaps inhalation exposure to the notified chemical (at ≤25% concentration) may occur during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. Exposure is expected to be minimised through the use of mechanical ventilation and/or enclosed systems and through the use of personal protective equipment such as coveralls, safety glasses and impervious gloves.

Exposure to the notified chemical in end-use products (at ≤25% concentration) may occur in professions where the services provided involve the application of cosmetic and personal care products to clients (e.g. hair dressers, workers in beauty salons) or in the cleaning industry. Such professionals may use some personal protective equipment to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified chemical.

6.1.2. Public Exposure

There will be widespread and repeated exposure of the public to the notified chemical (at ≤25% concentration) through the use of the household cleaning products and the rinse-off and leave-on cosmetic and personal care products. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray.

6.2. Human Health Effects Assessment

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

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 >2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test	evidence of sensitisation
Human, skin sensitisation – RIPT (1%)	no evidence of sensitisation
Human, skin sensitisation – RIPT (5%)	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics, metabolism and distribution.
Based on the water solubility (4.93 g/L at 21 °C), partition co-efficient (log Pow = 2.5 at 22.5 °C) and the low molecular weight (<500 Da) of the notified chemical, passive diffusion across the gastrointestinal (GI) tract and dermal absorption are expected to occur. The notified chemical may also be absorbed across the respiratory tract.

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

Irritation and Sensitisation.
In a skin irritation study in rabbits, very slight to well-defined erythema was noted in all animals, with the effects resolved within 72 hours. In an eye irritation study in rabbits, mild to moderate conjunctival irritation was noted, with treated eyes appearing normal after 48 hours. The irritation scores in these studies did not warrant classification of the chemical as a skin or eye irritant.

The notified chemical (at 100% induction concentration; 100% challenge concentration) was found to be a sensitiser in guinea pigs (Magnusson-Kligman method), with discrete/patchy to moderate/confluent erythema noted in 5/10 and 3/10 animals at 24 and 48 hours after patch removal, respectively.

The notified chemical (at 1% and 5% concentration) was determined by the study authors to not be a skin sensitiser in human repeat insult patch studies. However, it is noted that minimal or doubtful responses were noted in 2 and 1 subjects at 24 and 48 hours, respectively, following challenge patch removal (5% concentration) and in 1 subject at 24 hours following challenge patch removal (1% concentration).

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

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

Health hazard classification
Based on the 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 following table.

Hazard classification	***Hazard statement***
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):
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 ≤25% concentration) may occur during blending operations. The notified chemical is considered to be a skin sensitiser and products containing it at concentrations ≥1% are classified as such, therefore caution should be exercised when handling the notified chemical at concentrations ≥1%. Therefore, provided that control measures are in place to minimise worker exposure, including the use of automated processes and PPE, the risk to the health of workers from use of the notified chemical is not

considered to be unreasonable.

End-use
Cleaners and beauty care professionals will handle the notified chemical at ≤25% concentration, similar to public use. Therefore, the risk to workers who regularly use products containing the notified chemical is expected to be of a 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.

6.3.2. Public Health

Skin sensitisation
The main risk associated with use of the notified chemical at ≤1.15% concentration in fine fragrances, ≤2.5% in other cosmetic products and ≤25% in household cleaning products, is its potential to cause sensitisation by skin contact.

Methods for the quantitative risk assessment for dermal sensitisation have been proposed and been the subject of significant discussion (see for example, Api *et al.*, 2008 and RIVM, 2010). As is shown in the table below, the Consumer Exposure Level (CEL) from use of the notified chemical in a number of different cosmetic and household cleaning products may be estimated (SCCS, 2010; RIVM, 2006). When tested at between 1 and 5% concentration in human repeat insult patch studies (0.2 mL applied to 2 cm x 2 cm patches), the notified chemical was determined by the study authors to not be a skin sensitiser. Consideration of the details of the studies (including the minimal/doubtful responses that were noted at challenge), and application of appropriate safety factors, allowed the derivation of an Acceptable Exposure Level (AEL) of 1.6 μg/cm^2 (derived from the study conducted at 1% concentration). In this instance, the factors employed included an intraspecies factor (10), a matrix factor (3.16), a use and time factor (3.16) and a database uncertainty factor (3.16), giving an overall safety factor of >300 (300 used for calculations).

Product type	Proposed usage concentration (%)	CEL chemical (μg/cm^2)	AEL chemical (μg/cm^2)	Recommended usage concentration (%)
Deodorant spray	2.5	179	1.6	≤0.02
Fine fragrances	1.15	43	1.6	≤0.04
Other leave-on cosmetics (assumed: face cream)	2.5	68	1.6	≤0.06
Rinse-off cosmetics (assumed: hand wash soap)	2.5	5.8	1.6	≤0.7
Household cleaning products (assumed: cleaning liquid)	25	43	1.6	≤0.9

As the CEL>AEL, the risk to the public of the induction of sensitisation that is associated with the use of the notified chemical in deodorants (at ≤2.5%), fine fragrances (at ≤1.15%), other leave-on cosmetic products (using face cream as a worst case example; at ≤2.5%), rinse-off cosmetic products (using hand wash soap as a worst case example; at ≤2.5%) and household cleaning products (using cleaning liquid as a worst case example; at ≤25%) is considered to be unreasonable. Reducing the concentration of the notified chemical in deodorants to ≤0.02%, fine fragrances to ≤0.04%, other leave-on cosmetic products to ≤0.06%, rinse-off cosmetic products to ≤0.7% and household cleaning products to ≤0.9% allows recalculation of the consumer exposure to acceptable levels. 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.

Repeated 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 (revised) concentration 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 ≤0.02% in deodorants, ≤0.04% in fine fragrances, ≤0.06% in other leave-on cosmetic products, ≤0.7% in rinse-off cosmetic products and ≤0.9% in household cleaning products, is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported as a component of fragrance preparations for local reformulation. Potential release during reformulation in Australia is 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 will be collected with inert material and disposed of to landfill. Import containers will either be recycled or disposed of through an approved waste management facility. Therefore, up to 0.2% of the import volume is estimated to be released to landfill as a result of reformulation in Australia.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be released to sewers in domestic situations across Australia as a result of its use in cosmetic products that will be washed off the hair and skin, and the use and disposal of household cleaning products.

RELEASE OF CHEMICAL FROM DISPOSAL

It is estimated that a maximum of 3% of the consumer product containing 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

The notified chemical is moderately volatile and it is expected that some will partition to air during use, which is a functional requirement for fragrances. The half-life of the notified chemical in air was calculated to be 17 h based on reactions with hydroxyl radicals (US EPA assessment, predicted). The notified chemical is therefore not expected to persist in the air compartment.

Following its use in Australia, the majority of the notified chemical will enter the aquatic compartment, with the majority discharged into sewer systems. The notified chemical is readily biodegradable (US EPA assessment, measured, OECD 301D). Up to 89% is predicted to be removed in sewage treatment plants mostly through biodegradation (SimpleTreat; European Commission, 2003). In the case of release to surface waters, the notified chemical is expected to disperse and degrade via biotic and abiotic processes, or partition to air. The notified chemical is not likely to bioaccumulate, based on its low molecular weight and low bioconcentration factor (log BCF = 1.2, US EPA assessment, predicted).

A small proportion of notified chemical may be applied to land when effluent is used for irrigation or when sewage sludge is used for soil remediation. Notified chemical residues in landfill, soil and sludge are expected to degrade to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The following Predicted Environmental Concentrations (PEC) have been calculated assuming that all of the imported quantity of notified chemical will be released to sewer. Of this, an estimated 3% of the notified chemical is predicted to partition to the air compartment, 82% is predicted to degrade, and a further 3% is predicted to be removed by sewage treatment plant (STP) processes through adsorption to sludge (SimpleTreat; European Commission, 2003) before discharge to surface waters on a nation wide basis.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	89%	Mitigation
Daily effluent production:	4,523	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	

PEC - River:	0.07	µg/L
PEC - Ocean:	0.01	µg/L

Based on the Simple Treat modelling prediction of 3% partitioning to sludge, partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 0.182 mg/kg (dry wt). Biosolids are applied to agricultural soils, with an assumed average rate of 10 t/ha/year. Assuming a soil bulk density of 1500 kg/m^3 and a soil-mixing zone of 10 cm, the concentration of the notified chemical may approximate 0.001 mg/kg in applied soil. This assumes that degradation of the notified chemical occurs in the soil within 1 year from application. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated biosolids application, the concentration of notified chemical in the applied soil in 5 and 10 years may approximate 0.005 mg/kg and 0.01 mg/kg, respectively.

Notified chemical that is not removed from waste water during STP processes may be released to the environment in STP effluent. STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.073 µg/L may potentially result in a soil concentration of approximately 0.4846 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 2.423 µg/kg and 4.846 µg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity data were submitted. Modelled estimates for acute and chronic endpoints for aquatic organisms were provided in the US EPA assessment and are summarised below.

Endpoint	*Result*	*Assessment Conclusion*
Acute Toxicity		
Fish Toxicity	96 h LC50 = 16.0 mg/L	Harmful to fish
Daphnia Toxicity	48 h EC50 = 63.0 mg/L	Harmful to aquatic invertebrates
Algal Toxicity	96 h EC50 = 1.3 mg/L	Toxic to algae
Chronic Toxicity		
Fish Toxicity	ChV = 4.9 mg/L	Not harmful to fish with long lasting effects
Daphnia Toxicity	ChV = 6.3 mg/L	Not harmful to aquatic invertebrates with long lasting effects
Algal Toxicity	ChV = 1.0 mg/L [1]	Harmful to algae with long lasting effects

[1] ChV = (LOEC × NOEC)^{½} and, by definition, NOEC<LOEC. Therefore, the algal toxicity NOEC for the notified chemical is <1.0 mg/mL

Based on the estimated endpoints in the absence of experimental data, under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009), the notified chemical is toxic to algae and harmful to fish and aquatic invertebrates, and is formally classified as 'Acute Category 2: Toxic to aquatic life'. The notified chemical is considered not harmful to fish and aquatic invertebrates for long-term hazard and harmful to algae with long lasting effects. In the absence of experimental data, the notified chemical is formally classified under the GHS on the basis of its estimated chronic toxicity as 'Chronic Category 3: Harmful 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 chronic algae toxicity of the notified chemical and an assessment factor of 100. A more conservative assessment factor of 100 is appropriate in this case to account for uncertainty of the applicability the chemical class (ester) used in the QSAR prediction, and, the use chronic endpoints as provided in the US EPA assessment (ChV = (LOEC × NOEC)^{½}) which are not no-observed effect concentrations (NOECs).

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
ChV50 (Algae)	1.00	mg/L
Assessment Factor	100	
PNEC:	10.00	µg/L

7.3. Environmental Risk Assessment

Based on the above PEC and PNEC values, the following Risk Quotient (Q) has been calculated:

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.07	10	0.007
Q - Ocean	0.01	10	0.001

The majority of the notified chemical will be disposed of to sewer. The notified chemical is unlikely to reach ecotoxicologically significant concentrations in the aquatic environment based on its annual importation quantity and the partial removal of the chemical from waste water via biodegradation, volatilisation and sorption to sewage sludge. The notified chemical has a low potential for bioaccumulation and is unlikely to persist in the aquatic or air compartments. The risk quotient (PEC/PNEC) is well below 1 for both riverine and oceanic discharge scenarios. Therefore, at the maximum importation volume, the notified chemical is not considered to pose an unreasonable risk to the environment when used as described.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Freezing Point <-81 ºC

Method OECD TG 102 Melting Point/Melting Range.
EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks Determined by placing the test substance in a freezer (-81 ºC) for 2 hours. The substance did not show any indication of freezing.
Test Facility Notox (1999a)

Boiling Point 186-187 ºC

Method OECD TG 103 Boiling Point.
EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks Determined by differential scanning calorimetry (DSC). The observed boiling temperature was not corrected to standard atmospheric pressure.
Test Facility Notox (1999b)

Density 967 kg/m^3 at 20 ± 0.5 ºC

Method Similar to OECD TG 109 Density of Liquids and Solids.
Remarks Determined using an oscillating densitometer. Non-GLP-compliant study.
Test Facility Firmenich (2011)

Water Solubility 4.93 g/L at 21 ºC

Method OECD TG 105 Water Solubility.
EC Directive 92/69/EEC A.6 Water Solubility.
Remarks Flask Method/GC-FID
Test Facility Notox (1999c)

Hydrolysis as a Function of pH

Method In house

pH	T (°C)	$t_{½}$
2	40	6 days
5	40	2 days
7	40	<1 day
8.5	40	<1 day
12	40	<1 hour

Remarks 0.001 M notified chemical in buffer solutions (types A, C, D, F and I: Reference Handbook of Chemistry and Physics) with 1% non-ionic surfactant. GC-FID determination at day 1, 2, 4, 7, 15, 21 and 28.
Test Facility Unspecified

Partition Coefficient (n-octanol/water) log Pow = 2.5 at 22.5 ºC

Method OECD TG 117 Partition Coefficient (n-octanol/water).
EC Directive 92/69/EEC A.8 Partition Coefficient.
Remarks HPLC Method. Stationary phase: C18 column; mobile phase: 40:60 (v/v) acetonitrile/water; reference standards: n=5, r=0.989, Log Pow 1.1-3.4.
Test Facility Notox (1999d)

Flash Point 65 ºC at 101.3 kPa

Method EC Directive 92/69/EEC A.9 Flash Point.
Remarks Determined using a Pensky-Martens closed cup apparatus

Test Facility Notox (1999e)

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) BR
Vehicle None
Remarks - Method No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	3F	2000	0
II	3M	2000	0

LD50 >2000 mg/kg bw
Signs of Toxicity In all male rats, lethargy was noted on the day of treatment. In addition, a ~15% body weight loss in males was recorded 7-days post-treatment, the animals recovered thereafter.
Effects in Organs None

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

TEST FACILITY Notox (1999f)

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 72 hours
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	0.7	0.7	1	2	<72 hours	0
Oedema	0	0	0	0	-	0

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

Remarks - Results Very slight to well-defined erythema was noted in all animals (at up to and including the 48-hour observation).

CONCLUSION The notified chemical is slightly irritating to the skin.

TEST FACILITY Notox (1999g)

B.3. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3
Observation Period 72 hours
Remarks - Method No significant protocol deviations.

Following the 24-hour observation a 2% aqueous fluorescein solution was instilled into both eyes of each animal.

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	0.3	0.3	0.3	2	<48 hours	0
Conjunctiva: chemosis	0	0	0	2	<24 hours	0
Conjunctiva: discharge	0	0	0	1	<24 hours	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	-	0

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

Remarks - Results No corneal or iridial effects were reported. Slight to moderate conjunctival irritation was noted in the treated eyes of all animals, with the eyes appearing normal after 48 hours.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY Notox (1999h)

B.4. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD OECD TG 406 Skin Sensitisation - Magnusson and Kligman guinea pig maximisation test.
Species/Strain Albino guinea pig/Dunkin Hartley
PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: 20%
topical: 100%
MAIN STUDY
Number of Animals Test Group: 10F Vehicle Control Group: 5F
INDUCTION PHASE Induction Concentration:
intradermal: 20%
topical: 100%
Signs of Irritation Following the intradermal and topical induction phases, minimal-moderate irritation at the induction sites was noted.
CHALLENGE PHASE
1st challenge topical: 100%,
Remarks - Method No significant protocol deviations.
The vehicle was corn oil.
The test sites were treated with sodium dodecyl sulfate prior to the topical induction phase.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: 1st challenge*	
		24 h	*48 h*
Test Group	100%	5/10	3/10
	0%	2/10	1/10

Control Group	100%	0/5	0/5
	0%	0/5	0/5

Remarks - Results: Discrete/patchy erythema to moderate/confluent erythema was noted in 5/10 and 3/10 animals at 24 and 48 hours after patch removal, respectively. In 2/10 experimental animals a response was also noted at the vehicle-treated site and was considered to have occurred by accident (leakage from adjacent treated sites).

CONCLUSION: There was evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY: Notox (1999i)

B.5. Skin sensitisation – human volunteers

TEST SUBSTANCE: Notified chemical (1% in vehicle)

METHOD: Repeated insult patch test with challenge

Study Design: Induction Procedure: Patches containing 0.2 mL test substance were applied 3 times per week (Monday, Wednesday and Friday) 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 for patches applied on Friday).
Rest Period: 12-14 days
Challenge Procedure: A patch was applied to a naïve site. Patches were removed by the applicants after 24 h. Sites were graded 24 and 48 h post-patch removal.

Study Group: 93 F, 26 M; age range 19-75 years

Vehicle: Diethyl phthalate

Remarks - Method: Occluded. The test substance was spread on a 2 cm x 2 cm patch.

RESULTS

Remarks - Results: 101/119 subjects completed the study. 11/119 subjects were discontinued for failure to keep to the scheduled visits (0-8 induction observations recorded), 6/119 voluntarily withdrew (0-3 induction observations recorded) and 1/119 was discontinued due to an adverse event that was reportedly non-product related (rash noted in the patch area during induction, which cleared within two days; subject was noted to not have exhibited a rash at challenge).

Definite erythema (no edema) was noted for 1 subject/application, following induction applications 2 and 9. A minimal or doubtful response was noted for 1, 1 and 2 subjects/application following induction applications 2, 3 and 6, respectively.

A minimal or doubtful response was noted for 1 subject 24 h following challenge patch removal.

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

TEST FACILITY: TKL (1999)

B.6. Skin sensitisation – human volunteers

TEST SUBSTANCE: Notified chemical (5% in vehicle)

METHOD: Repeated insult patch test with challenge

Study Design: Induction Procedure: Patches containing 0.2 mL test substance were applied 3 times per week (Monday, Wednesday and Friday) 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 for patches applied on Friday). Rest Period: 10-15 days Challenge Procedure: A patch was applied to a naïve site. Patches were removed by the applicants after 24 h. Sites were graded 24 and 48 h post-patch removal.
Study Group	92 F, 17 M; age range 18-74 years
Vehicle	Diethyl phthalate
Remarks - Method	Occluded. The test substance was spread on a 2 cm x 2 cm patch.

RESULTS

Remarks - Results	98/109 subjects completed the study. 6/109 subjects were discontinued for failure to keep to the scheduled visits and 5/109 voluntarily withdrew. No induction observations were recorded for 7 of these subjects and 3-9 observations were recorded for the remaining 4 subjects that did not complete the study. A minimal or doubtful response was noted for 1 subject/application following induction applications 4 and 8. A minimal or doubtful response was noted for 2 and 1 subject, 24 h and 48 h following challenge patch removal, respectively.

CONCLUSION	The test substance was non-sensitising under the conditions of the test.
TEST FACILITY	TKL (2001)

B.7. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	Aroclor 1254-induced rat liver (S9 homogenate)
Concentration Range in Main Test	a) With metabolic activation: 100, 333, 1000, 3330 and 5000 µg/plate b) Without metabolic activation: 100, 333, 1000, 3330 and 5000 µg/plate
Vehicle	Dimethyl sulphoxide
Remarks - Method	A range-finding study was conducted using 8 concentrations of the test substance, assayed in triplicate against strains TA100 and WP2uvrA (3-5000 µg/plate). This formed part of Test 1. Vehicle and positive controls were used in parallel with the test material. Positive controls: i) without S9: sodium azide (TA1535), 9-aminoacridine (TA1537), daunomycine (TA98), methylmethanesulfonate (TA100) and 4-nitroquinoline-N-oxide (WP2uvrA); ii) with S9: 2-aminoanthracene (all strains).

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	>5,000	>5,000	Negative
Test 2	>5,000	>5,000	Negative
Present			
Test 1	>5,000	>5,000	Negative
Test 2	>5,000	>5,000	Negative

Remarks - Results	The test substance did not cause a visible reduction in the growth of the bacterial background lawn at any dose level. No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains up to and including the maximum dose, either with or without metabolic activation. The positive controls gave satisfactory responses, confirming the validity of the test system.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Notox (1999j)

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