File No: LTD/2001

November 2017

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

1,3-Dioxolane, 2-methyl-4-phenyl-

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 and Energy.

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:

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Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/2001	Symrise Pty Ltd	1,3-Dioxolane, 2-methyl-4-phenyl-	ND*	< 1 tonne per annum	Fragrance ingredient

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical cannot be classified according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia.

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 3	H402 – Harmful to aquatic life
Chronic 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 in the proposed manner, the notified chemical is not considered to pose an unreasonable risk to public health.

Environmental risk assessment
On the basis of the PEC/PNEC ratio and the reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical during reformulation:
  − Enclosed, automated processes, where possible
  − Adequate 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 reformulation:
  − Avoid contact with skin
  − Avoid inhalation

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

- Impervious gloves
- Coveralls

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

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

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

Disposal

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

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 0.3% in 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.

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

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Symrise Pty Ltd (ABN: 67 000 880 946)
168 South Creek Road
DEE WHY NSW 2099

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
No details are claimed exempt from publication.

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

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT
Low Volume Chemical Permit

NOTIFICATION IN OTHER COUNTRIES
EU (2016)

2. IDENTITY OF CHEMICAL

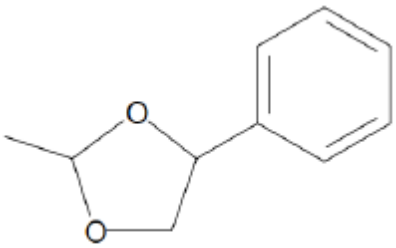
MARKETING NAME
JACINTHAFLOR

CAS NUMBER
33941-99-0

CHEMICAL NAME
1,3-Dioxolane, 2-methyl-4-phenyl-

MOLECULAR FORMULA
$C_{10}H_{12}O_2$

STRUCTURAL FORMULA



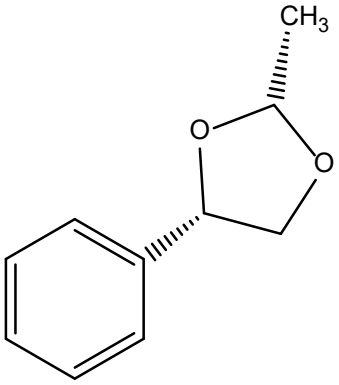
MOLECULAR WEIGHT
164.2 g/mol

ANALYTICAL DATA
Reference NMR, FT-IR, GC-MS, LC-MS, GC, UV-VIS spectra and optical activity measurement were provided.

3. COMPOSITION

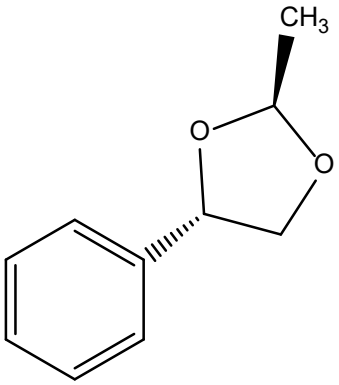
DEGREE OF PURITY
> 99%

The notified chemical is a racemic mixture of four stereoisomers (2 diastereoisomers and 2 enantiomers) in roughly equimolar proportions.



+ Enantiomer

Chemical Name: 1,3-Dioxolane, 2-methyl-4-phenyl-, (2R,4S)-*rel*- (56.2%)
CAS number: 58345-31-6



+ Enantiomer

Chemical Name: 1,3-Dioxolane, 2-methyl-4-phenyl-, (2R,4RS)-*rel*- (43.7%)
CAS number: 58345-15-6

HAZARDOUS IMPURITIES
None

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% BY WEIGHT)
None

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless, clear liquid

Property	Value	Data Source/Justification
Melting Point	< -100 °C	Measured
Boiling Point	Decomposes without boiling at 110 °C	Measured
Density	1,070 kg/m^3 at 20 °C	Measured
Vapour Pressure	10.9 kPa at 25 °C	Measured
Water Solubility	2.57 g/L at 20 °C and pH 4.0	Measured
Hydrolysis as a Function of pH	Not determined	The notified chemical is unlikely to hydrolyse within environmental pH range (4 – 9)
Partition Coefficient (n-octanol/water)	log Pow = 2.19 at 25 °C	Measured
Adsorption/Desorption	log K_{oc} = 1.91 – 1.96	Estimated (KOCWIN v 2.00, US EPA 2011)
Dissociation Constant	Not determined	The notified chemical does not contain any dissociable functionalities
Flash Point	97.5 °C at 101.3 kPa (closed cup)	Measured
Flammability	Not flammable	Expert statement from flash point study
Autoignition Temperature	400 °C	Measured
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidative properties

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

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

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is 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 as a component of finished consumer products such as fine fragrances, other cosmetic products and household cleaning products, at ≤ 0.3% concentration. The notified chemical may also be imported into Australia as a component of fragrance mixtures at ≤ 10% concentration, a solution of the notified chemical at ≤ 10% concentration and in its neat form.

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

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

IDENTITY OF MANUFACTURER/RECIPIENTS
Symrise Pty Ltd (the notifier)

PACKAGING
Finished products containing the notifed chemical at ≤ 0.3% concentration and solutions containing the notified chemical at ≤ 10% concentration will be imported in 30 L and 216 L closed lacquered metal drums. In addition, 30 L HDPE/EVOH plastic canisters may also be used. The neat notified chemical will be imported in 30 L HDPE/EVOH plastic containers.

Finished products containing the notified chemical at ≤ 0.3% concentration will be packaged in containers suitable for retail sale.

USE
The notified chemical will be used as a fragrance ingredient in cosmetic and household products at ≤ 0.3% concentration.

Concentration of the notified chemical in finished consumer products will be as follows:

Finished Consumer Product	*Final Concentration of the Notified Chemical (%)*
Fine fragrance	0.005 – 0.3
Other cosmetic products	0.002 – 0.05
Household cleaning products	0.002 – 0.09

OPERATION DESCRIPTION
Reformulation of the notified chemical or fragrance mixtures containing the notified chemical at ≤ 10% concentration into finished consumer goods may vary depending of the type of product produced and may involve both automated and manual transfer steps. Typically, reformulation processes may incorporate blending operations that are highly automated and occur in a fully enclosed/contained environment, followed by automated filling of the reformulated end-use products into containers of various sizes.

End-use products containing the notified chemical (at ≤ 0.3% concentration) will be used by consumers and professionals such as hairdressers, beauticians and cleaners. Depending on the nature of the product, these could be applied in a number of ways, such as by hand, using an applicator or sprayed.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and warehouse	None	Incidental
Mixer	4	2
Drum handling	4	2
Drum cleaning/washing	4	2
Maintenance	4	2
Quality control	0.5	2
Packaging	4	2
End users (professionals)	1 - 8	200

EXPOSURE DETAILS
Transport and storage
Transport, storage and warehouse workers may come into contact with the notified chemical in its neat form, at ≤ 10% concentration (in solutions or fragrance mixtures) or at ≤ 0.3% concentration (in final formulated products), only in the event of accidental rupture of containers.

Formulation of end products
During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified chemical in its neat form or at ≤ 10% concentration may occur during handling of drums, during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. The notifier states that exposure is expected to be minimised through the use of mechanical ventilation and/or enclosed systems, and through the use of PPE such as protective clothing, eye protection and suitable gloves.

End use professionals
Exposure to the notified chemical at ≤ 0.3% concentration in end-use products may occur in professions where the services provided involve the application of cosmetic products to clients or the use of household products in the cleaning industry. The principal route of exposure will be dermal, while ocular and inhalation exposure is

also possible. Such professionals may use some PPE to minimise repeated exposure and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or less extent than that experienced by consumers using products containing the notified chemical.

6.1.2. Public Exposure

There will be widespread and repeated exposure of the public to the notified chemical (at ≤ 0.3% concentration) through the use of the cosmetic and household products. The main route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray.

Data on typical use patterns of product categories in which the notified chemical may be used are shown in the following table (SCCS, 2012; ACI, 2010). For the purposes of the exposure assessment via the dermal route, Australian use patterns for the various product categories were assumed to be similar to those in Europe. In the absence of dermal absorption data, a dermal absorption (DA) of 100% was assumed for the notified chemical (ECHA, 2014). A lifetime average female body weight (BW) of 64 kg (enHealth, 2012) was used for calculation purposes.

Cosmetic products (dermal exposure)

Product Type	**Amount** (mg/day)	**Max. Intended Conc.** (%)	**Retention Factor** (unitless)	**Daily Systemic Exposure** (mg/kg bw/day)
Body lotion	7820	0.05	1.000	0.06109
Face cream	1540	0.05	1.000	0.01203
Hand cream	2160	0.05	1.000	0.01688
Fine fragrances	750	0.30	1.000	0.03516
Deodorant (non-spray)	1500	0.05	1.000	0.01172
Shampoo	10460	0.05	0.010	0.00082
Conditioner	3920	0.05	0.010	0.00031
Shower gel	18670	0.05	0.010	0.00146
Hand wash soap	20000	0.05	0.010	0.00156
Hair styling products	4000	0.05	0.100	0.00313
Total				0.14414

Daily systemic exposure = (Amount × Max. Intended Conc. × Retention Factor × Dermal Absorption) / Body Weight

Household products (indirect dermal exposure)

Product type	**Amount** (g/use)	**Max. Intended Conc.** (%)	**Product Retained** (%)	**Transfer** (%)	**Daily systemic exposure** (mg/kg bw/day)
Laundry liquid	230	0.09	0.95	10	0.00307
Fabric softner	90	0.09	0.95	10	0.00120
Total					0.00428

Daily systemic exposure = (Amount × Max. Intended Conc. × Product Retained × Transfer × Dermal Absorption) / Body Weight

Household products (dermal exposure)

Product type	**Frequency** (use/day)	**Max Intended Conc** (%)	**Product Use Conc** (g/cm^3)	**Time Scale Factor** (unitless)	**Daily systemic exposure** (mg/kg bw/day)
Laundry liquid	1.43	0.09	0.01	0.007	0.00003
Dishwashing liquid	3	0.09	0.009	0.03	0.00023
All-purpose cleaner	1	0.09	1	0.007	0.00195
Total					0.00220

Daily systemic exposure = (Frequency × Max. Intended Conc. × Contact Area (not shown) × Product Use Conc. × Film Thickness (not shown) × Time Scale Factor × Dermal Absorption) / Body Weight

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above table that contain the notified chemical at the maximum intended concentrations as specified by the notifier in various product types. This would result in a combined internal dose of 0.151 mg/kg bw/day.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the following table. For full details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rabbit, skin irritation	slightly irritating
Human, skin irritation – 48 hour patch test	non-irritating
Eye irritation (*in vitro*) - BCOP	non-irritating
Guinea pig, skin sensitisation –adjuvant test	no evidence of sensitisation
Human, skin sensitisation – RIPT (100%)	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non-mutagenic

Toxicokinetics

Given the low molecular weight of the notified chemical (164 Da), there is potential for absorption across biological membranes.

Acute toxicity

The notified chemical is of low acute oral toxicity based on a study conducted in rats.

Irritation and sensitisation

The notified chemical was found to be slightly irritating to skin in a study conducted in rabbits. In a 48 hour human patch test completed on 53 subjects, the notified chemical at 100% concentration was found to be non-irritating.

In the skin irritation study conducted in rabbits, all animals displayed very slight erythema one hour after application which continued in 2/3 animals up to the 72 hour observation accompanied by loss of skin elasticity. No animals displayed erythema by Day 7, but 2/3 animals showed slight desquamation. All animals displayed very slight oedema at the one hour observation, and continued in 2/3 animals for up to 24 hours. One animal displayed very slight oedema for up to 72 hours after exposure to the test substance.

In an *in vitro* bovine corneal opacity and permeability (BCOP) test, the notified chemical was determined not to be irritating to eyes.

In a guinea pig maximisation test, the notified chemical did not show evidence of skin sensitisation when tested up to 100% concentration. In a human repeat insult patch test (HRIPT) completed on 104 subjects, the notified chemical at 100% concentration did not elicit a positive sensitisation response.

Mutagenicity/Genotoxicity

The notified chemical tested negative in a bacterial reverse mutation assay with Salmonella Typhimurium and Escherichia Coli strains.

Health hazard classification

Based on the available information, the notified chemical cannot be classified according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Based on the available information the notified chemical is of low hazard presenting only as a slight skin irritant. The notified chemical has the potential to cross biological membranes; however, the toxicity of the notified chemical following repeated exposure is unknown.

Reformulation
During reformulation, workers may be at risk of slight skin irritation effects and potential systemic effects from repeated exposure when handling the notified chemical in its neat form. The notifier anticipates that worker exposure will be limited through the use of engineering controls such as enclosed systems, automated processes and local exhaust ventilation. The use of appropriate PPE (coveralls, imperious gloves and eye protection) will also be used to limit worker exposure.

End-Use
End use professionals such as be beauticians, hairdressers and cleaners may be exposed to the notified chemical at ≤ 0.3% concentration. Dermal, and to a lesser extent, ocular and inhalation exposure may occur. PPE may be employed by workers to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, the risk to such workers is expected to be of a similar or lesser extent than that for consumers using the various products containing the notified chemical.

Therefore, under the occupational settings described, the risk to the health of workers from use of the notified chemical is not considered to be unreasonable.

6.3.2. Public Health
Members of the public will experience widespread and frequent exposure to the notified chemical at ≤ 0.3% concentration through daily use of cosmetic and household products. The main route of exposure is expected to be dermal and inhalation, with some potential for accidental ocular or oral exposure.

Local Effects
The notified chemical is slightly irritating to the skin. Given the low proposed use concentration (≤ 0.3%), irritation effects are not expected.

Systemic Effects
No repeated dose toxicity was provided for the notified chemical. However, exposure is expected to be limited by the low concentration of the notified chemical (≤ 0.3%) in end use products (see Section 6.1.2).

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at ≤ 0.3% concentration in 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 into Australia in its neat form, as a component of fragrance mixtures or in solution for reformulation into finished cosmetic and household cleaning products, or as a component of finished cosmetic and household cleaning products. There is unlikely to be any significant release of the notified chemical to the environment from transport and storage, except in the case of accidental spills and leaks. In the event of spills, the products containing the notified chemical is expected to be collected with absorbents, and disposed of to landfill in accordance with local government regulations.

The reformulation process will involve blending operations that will be highly automated, and is expected to occur within a fully enclosed environment followed by automated filling of the reformulated end-use products into containers of various sizes. Wastes containing the notified chemical generated during reformulation include equipment wash water (estimated to be < 1% of the import volume by the notifier), residues in empty import containers and spilt materials. Wash waters are expected to be released to on-site waste water treatment processes, or sewers in a worst case scenario. Empty import containers and residues are expected to be recycled or disposed of through licensed waste management services.

RELEASE OF CHEMICAL FROM USE
The notified chemical is expected to be released to the aquatic compartment through sewers during its use in cosmetic and household cleaning products across Australia.

RELEASE OF CHEMICAL FROM DISPOSAL

Wastes and residues of the notified chemical in empty end-use containers are likely to either share the fate of the container and be disposed of to landfill, or be released to the sewer system when containers are rinsed before recycling 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 be released to sewers on a nationwide basis. The submitted biodegradation study indicates that the notified chemical is not expected to be rapidly degraded in sewage treatment plants (STPs). For the details of the environmental fate study please refer to Appendix C.

Volatilization of the notified chemical is expected to be limited based on Henry's Law constant (6.86 × 10-5 atm-m3/mole). The half-life of the notified chemical in air is calculated to be 5.55 h based on reactions with hydroxyl radicals (AOPWIN v1.92, US EPA 2011). Therefore, any notified chemical released to the atmospheric compartment is not expected to persist.

In STPs a significant proportion of the notified chemical is expected to remain in the aqueous phase based on its high water solubility and moderate partition coefficient. Therefore, a significant proportion of the notified chemical may be released to surface waters. A 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. The notified chemical has low potential to bioaccumulate based on its octanol-water partition coefficient value (log P_{OW} < 4.2). In the aquatic and soil compartments, the notified chemical is expected to eventually degrade through biotic and abiotic processes to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The calculation for the predicted environmental concentration (PEC) is summarised in the table below. Based on the reported use in cosmetic and household cleaning products, it is assumed that 100% of the total import volume of the notified chemical is released to the sewer. The release is assumed to be nationwide over 365 days per year. It is conservatively assumed that there is no removal of the notified chemical during sewage treatment processes.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	0%	
Daily effluent production:	4,877	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.56	µg/L
PEC - Ocean:	0.06	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m2/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/m3). Using these assumptions, irrigation with a concentration of 0.56 µg/L may potentially result in a soil concentration of approximately 3.75 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 18.7 µg/kg and 37.5 µg/kg, respectively.

7.2. Environmental Effects Assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Daphnia Toxicity	48 h EC50 > 100 mg/L	Not harmful to aquatic invertebrates
Algal Toxicity	72 h EC50 = 69.2 mg/L NOEC = 50 mg/L	Harmful to algae

Based on the acute ecotoxicological endpoints, the notified chemical is expected to be harmful to algae. Therefore, the notified chemical is classified as "Acute Category 3: Harmful to aquatic life" according to the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations 2009). On the basis of acute toxicity data and lack of biodegradability, the notified chemical is formally classified as 'Chronic Category 3: Harmful to aquatic life with long lasting effects".

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentrations (PNEC) for the notified chemical have been derived from the most sensitive endpoint (NOEC) for algae and an assessment factor of 500 is applied as two measured acute toxic endpoints and one chronic endpoint are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
NOEC (alga)	50.00	mg/L
Assessment Factor	500	
Mitigation Factor	1.00	
PNEC:	100.00	µg/L

7.3. Environmental Risk Assessment

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.56	100	0.006
Q - Ocean	0.06	100	0.001

The Risk Quotients (Q = PEC/PNEC) for discharge of treated effluents containing the notified chemical have been calculated to be < 1 for both river and ocean compartments indicating that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in surface waters based on its maximum annual importation quantity. On the basis of the PEC/PNEC ratio and assessed use pattern in cosmetic formulations 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 < 100 °C

Method	OECD TG 102 Melting Point/Melting Range EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature
Remarks	Differential scanning calorimetry method used. The test item did not freeze when cooled to -100 °C.
Test Facility	consilab (2015a)

Boiling Point Decomposes without boiling at 110 °C

Method	OECD TG 103 Boiling Point EC Council Regulation No 440/2008 A.2 Boiling Temperature
Remarks	Differential scanning calorimetry method used. Test item decomposed at 110 °C before a boiling point could be detected.
Test Facility	consilab (2015a)

Density 1,070 kg/m^3 at 20 °C

Method	OECD TG 109 Density of Liquids and Solids EC Council Regulation No 440/2008 A.3 Relative Density
Remarks	Oscillated densitometer method used.
Test Facility	consilab (2015b)

Vapour Pressure 8.4 kPa at 20 °C
10.9 kPa at 25 °C
36.3 kPa at 50 °C

Method	OECD TG 104 Vapour Pressure OECD TG 113 Screening Test for Thermal Stability (1981) EC Council Regulation No 440/2008 A.4 Vapour Pressure
Remarks	Thermal stability of the test item was measured prior to determining its vapour pressure. Thermal stability measured using differential scanning calorimetry in a closed glass crucible under nitrogen heated up to 300 °C. No effects on thermal stability were observed. Vapour pressure measured using the dynamic method (vapour-liquid equilibrium).
Test Facility	consilab (2015c)

Water Solubility 2.57 g/L at 20 °C and pH 4.0

Method	OECD TG 105 Water Solubility EC Council Regulation No 440/2008 A.6 Water Solubility
Remarks	Flask Method. The pH was measured from three replicates and was not adjusted. No colloidal suspensions were detected.
Test Facility	Noack Laboratorien GmbH (2016a)

Partition Coefficient (n-octanol/water) log Pow = 2.19 at 25 °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	Noack Laboratorien GmbH (2016b)

Flash Point 97.5 °C at 101.3 kPa

Method	EC Council Regulation No 440/2008 A.9 Flash Point
Remarks	Closed cup method.
Test Facility	consilab (2015d)

Autoignition Temperature 400 °C at 100.8 kPa

Method	EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases)
Test Facility	consilab (2015e)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method (1996)
EC Council Regulation No 440/2008 B.1 tris Acute Oral Toxicity – Acute Toxic Class Method

Species/Strain	Sprague-Dawley Rat / CD (Crl:CD (SD) IGS BR)
Vehicle	None
Remarks - Method	No significant protocol deviations.

RESULTS

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

LD50	> 2000 mg/kg bw
Signs of Toxicity	One female animal and all male animals were comatose on the day of dosing. The female was found dead at four hours after dosing. All males recovered by the 24 hour time point. Noted signs of toxicity included ataxia, hunched posture, lethargy, piloerection, prostration, decreased respiratory rate, laboured respiration, ptosis, loss of righting reflex and splayed gait. All signs off toxicity were reversed at 2 days after dosing in females and 3 days after dosing in males.
Effects in Organs	No abnormalities detected at post-mortem. Necropsy was not performed on the female that died during the study due to a technical error.
Remarks - Results	One female animal died during the study. All surviving animals made expected body weight gains throughout the study.

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

TEST FACILITY: Safepharm (2000a)

B.2. Irritation – skin

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 404 Acute Dermal Irritation/Corrosion (1992)
EC Council Regulation No 440/2008 B.4 Acute Toxicity (Skin Irritation)

Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	None
Observation Period	7 days
Type of Dressing	Semi-occlusive
Remarks - Method	No significant protocol deviations.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	1.00	0	1.00	1.00	< 7 days	0
Oedema	1.00	0	0.33	1.00	< 7 days	0

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

Remarks - Results	All animals displayed very slight erythema at the one hour observation. This effect continued in 2/3 animals up to the 72 hour time point and was accompanied at this time point by loss of skin elasticity. These animals did not display erythema at day 7, but did present with slight desquamation. All animals displayed very slight oedema at the one hour observation, and continued in 2/3 animals for up to 24 hours. One animal displayed very slight oedema for up to 72 hours.
CONCLUSION	The notified chemical is slightly irritating to the skin.
TEST FACILITY	Safepharm (2000b)

B.3. Skin irritation – human volunteers

TEST SUBSTANCE	Notified chemical
METHOD	48 hour human patch test
Study Design	0.2 mL test substance was applied to a patch placed on the skin for 48 hours. The test site was evaluated immediately after patch removal and 24 hours after patch removal.
Study Group	40 F, 13 M; age range 27 - 79 years
Vehicle	None
Remarks - Method	Occluded patches were used. The test substance (0.2 mL) was spread on a ¾ inch × ¾ inch patch.
RESULTS	
Remarks - Results	53/53 subjects completed the study. No visible skin reaction was observed on any of the subjects.
CONCLUSION	The notified chemical was non-irritating under the conditions of the test.
TEST FACILITY	Consumer Product Testing Co. (2006a)

B.4. Irritation – eye (*in vitro*)

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 437 Bovine Corneal Opacity and Permeability Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage (2013)
Vehicle	None
Remarks - Method	No significant protocol deviations. Saline (0.9% NaCl in deionised water) was used as a negative control and 2-ethoxyethanol (99%) was used as a positive control.

RESULTS

Test material	*Mean opacities of triplicate tissues*	*Mean permeabilities of triplicate tissues*	*Mean IVIS*
Vehicle control	0.33	0.053	1.13
*Test substance**	0.67	0.010	0.81
*Positive control**	57.67	0.822	70.00

IVIS = *in vitro* irritancy score
*Corrected for background values

Remarks - Results	The controls gave satisfactory results confirming the validity of the test system.

CONCLUSION The notified chemical was considered to be non-irritating to the eye under the conditions of the test.

TEST FACILITY Envigo (2015)

B.5. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD OECD TG 406 Skin Sensitisation – Guinea Pig Maximisation Test
EC Directive 96/54/EC B.6 Skin Sensitisation - Guinea Pig Maximisation Test

Species/Strain Guinea pig/Dunkin Hartley

PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: < 1%
topical: 50%

MAIN STUDY

Number of Animals Test Group: 10 Control Group: 5

Vehicle Arachis oil BP

Positive control

INDUCTION PHASE Induction Concentration:
intradermal: 1% (in arachis oil BP)
topical: 100%

Signs of Irritation Intradermal induction produced discrete or patchy to moderate and confluent erythema at 24 hours after injection. This was followed by moderate and confluent or intense erythema and swelling by the 48 hour time point. Intradermal injection of the vehicle (arachis oil BP) produced no erythema or discrete or patchy erythema at both time points.

Topical induction produced discrete or patchy erythema in 7/10 animals at 1 hour after treatment. The same effect occurred in 4/10 animals at 48 hours after treatment. Control animals (blank patch applied – no vehicle or treatment) did not display any signs of irritation.

CHALLENGE PHASE

1st challenge topical: 75% (in arachis oil BP)

2nd challenge topical: 100%

Remarks - Method No significant protocol deviations.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*	
		24 h	*48 h*
Test Group	75%	0/10	0/10
	100%	0/10	0/10
*Control Group**	75%	0/4	0/4
	100%	0/4	0/4

* One control animal died between the induction and challenge phases.

Remarks - Results No skin reactions were observed after challenge with the test substance in any of the animals.

One control animal died between the induction and challenge phases (day 20). The authors of this study note that the cause of death was not determined but was thought not to be treatment related.

Body weight gains were comparable to those seen in the control group animals.

CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	Safepharm (2000c)

B.6. Skin sensitisation – human volunteers

TEST SUBSTANCE	Notified chemical
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 hours and graded after an additional 24 h (or 48 h for patches applied on Friday). Rest Period: approx. 14 days Challenge Procedure: A patch was applied to a naïve site. Patches were removed by the applicants after 24 h. Sites were graded immediately following and 48 h post-patch removal.
Study Group	84 F, 30 M; age range 17 - 78 years
Vehicle	None
Remarks - Method	Occluded patches were used. The test substance was spread on ¾ inch × ¾ inch patches.
RESULTS	
Remarks - Results	104/114 subjects completed the study. The authors of this study note that the remaining subjects discontinued their participation for various reasons, which were not related to the application of the test material. No visible skin reaction was observed on any of the subjects during the induction or challenge phases.
CONCLUSION	The notified chemical was non-sensitising under the conditions of the test.
TEST FACILITY	Consumer Product Testing Co. (2006b)

B.7. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test (1997) EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria (2008) Plate incorporation procedure (Preliminary Test 1) Pre incubation procedure (Test 2)
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, *E. coli*: WP2uvrA
Metabolic Activation System	S9 fraction from phenobarbital/β-napthoflavone-induced rat liver.
Concentration Range in Main Test	a) With metabolic activation: 10 – 5000 µg/plate b) Without metabolic activation: 10 – 5000 µg/plate
Vehicle	DMSO
Remarks - Method	No deviations from the study plan were noted.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 5000	-	> 5000	Negative
Test 2	-	≥ 2500	> 5000	Negative

Present				
Test 1	≥ 5000	-	≥ 5000	Negative
Test 2	-	≥ 2500	≥ 5000	Negative

Remarks - Results

No substantial increase in revertant colony numbers of any of the five tester strains was observed following treatment with the test substance at any dose level, in the presence or absence of metabolic activation. Positive controls performed as expected, confirming the validity of the test system.

CONCLUSION

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

TEST FACILITY

Harlan CCR (2015)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Theoretical oxygen demand (ThOD)
Remarks - Method	No significant deviations from the test guidelines were reported. The stock solution was prepared at a concentration of 1 g/L and was further diluted to give a final concentration of 2 mg/L.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
7	-14.2	7	69.7
14	-12.8	14	72.5
21	-12.8	21	66.5
28	-8.5	28	91.8

Remarks - Results	All validity criteria for the test were satisfied. The percentage degradation of the reference compound, sodium benzoate surpassed the threshold level of 60% within 14 days indicating the suitability of the inoculums. The toxicity control exceeded 25% biodegradation after 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. No degradation of the notified chemical was observed after 28 days
CONCLUSION	The notified chemical is not readily biodegradable
TEST FACILITY	Arbeitsgemeinschaft GAB Biotechnologie GmbH and IFU Umweltanalytik GmbH (2000)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test - Static EC Council Regulation No 440/2008 C.2 Acute Toxicity for Daphnia - Static
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	160 - 180 mg $CaCO_3$/L
Analytical Monitoring	High Performance Liquid Chromatography with a Diode Array Detector (HPLC-DAD)
Remarks - Method	No significant deviations from the test guidelines were reported. The stock solution of 100 mg/L was freshly prepared with dilution water and treated with ultrasound for 15 min and then stirred for 15 min at room temperature.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Control	< LOQ*	20	0	0
100	104 – 98.7	20	0	0

*LOQ = limit of quantification of the analytical method (2.00 mg test item/L)

EC50	> 100 mg/L at 48 hours
Remarks - Results	All validity criteria for the test were satisfied. The measured test item concentrations were within ± 20% of the nominal concentration. No effects on *Daphnia magna* were observed in either the control or treated group.
CONCLUSION	The notified chemical is not harmful to aquatic invertebrates.
TEST FACILITY	Noack Laboratorien GmbH (2016c)

C.2.2. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test EC Council Regulation No 440/2008 C.3 Algal Inhibition Test
Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: Part I: 6.25, 12.5, 25.0, 50.0, 100 mg/L Part II: 1.563, 3.125, 6.25, 12.5, 25.0 mg/L Actual: Test I 6.41-6.64, 13.3-13.6, 25.4-27.1, 50.4-53.9, 97.7-103 mg/L Test II: 1.59-1.60, 3.16-3.45, 6.51-6.80, 12.9-13.6, 25.3-28.2 mg/L
Auxiliary Solvent	None
Water Hardness	0.24 mmol $Ca^{2+}Mg^{2+}$/L
Analytical Monitoring	High Performance Liquid Chromatography with a Diode Array Detector (HPLC-DAD)
Remarks - Method	No significant deviations from the test guidelines were reported. The stock solution of 100 mg/L was freshly prepared with dilution water and stirred for 1 hour. Further test concentrations were prepared by diluting the 100 mg/L stock solution. No endpoint based on biomass could be accurately established in test I, due to a steep dose response. Therefore, EC50 (growth rate) was determined based on the results of Test I, and EC50 (biomass) was determined based on the results of Test I and II.

RESULTS

Biomass		*Growth*	
EC50	*NOEC*	*EC50*	*NOEC*
mg/L at 72 h	*mg/L*	*mg/L at 72 h*	*mg/L*
55.5 (95% CI 44.7 - 69.1)	3.125	69.2 (95% CI 68.9-69.6)	50

Remarks - Results	All validity criteria for the test were satisfied. The measured test item concentrations were within ± 20% of the nominal concentrations.
CONCLUSION	The notified chemical is harmful to alga.
TEST FACILITY	Noack Laboratorien GmbH (2016d)

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