File No: LTD/1927

March 2017

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Benzenepropanal, 2-methyl-4-(2-methylpropyl)-

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:

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/1927	Givaudan Singapore Pte Ltd	Benzenepropanal, 2-methyl-4-(2-methylpropyl)-	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*
Skin corrosion/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 phrases:

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 described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

Based on the available information, when used at ≤ 0.21% concentration in fine fragrances, at ≤ 0.15% concentration in other cosmetics or at ≤ 0.17% concentration in 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 assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:

- Skin corrosion/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 skin 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:
  - 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 handling of the notified chemical during reformulation:
  - Avoid contact with skin and eyes
  - Avoid inhalation

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical during reformulation:
  - Coveralls
  - Impervious gloves
  - Eye protection
  - Respiratory protection, if inhalation exposure may occur

  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.

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 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 0.21% in fine fragrances, 0.15% in other cosmetics or 0.17% in household products;

or

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

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

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

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Givaudan Singapore Pte Ltd (ABN: 79 368 011 578)
1 Pioneer Turn
Singapore 627576

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)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU (2015), Switzerland (2016), China (2016)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Nympheal

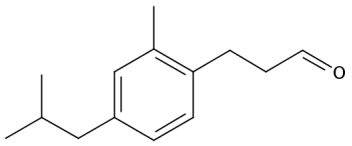
CAS NUMBER
1637294-12-2

CHEMICAL NAME
Benzenepropanal, 2-methyl-4-(2-methylpropyl)-

OTHER NAME(S)
GR-88-0778

MOLECULAR FORMULA
$C_{14}H_{20}O$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
204.31 Da

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

3. COMPOSITION

DEGREE OF PURITY
> 97%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
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: liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -50 °C	Measured
Boiling Point	284 °C at 101.3 kPa	Measured
Density	948 kg/m^3 at 20 °C	Measured
Vapour Pressure	1×10^{-4} kPa at 20 °C	Measured
Water Solubility	2.45×10^{-2} g/L at 20 °C	Measured
Hydrolysis as a Function of pH	pH 4 and 7, $t_{1/2}$ > 365 days pH 9, $t_{1/2}$ = 131.7 days	Measured
Partition Coefficient (n-octanol/water)	log Pow = 3.7 at 35 °C	Measured
Surface Tension	45.9 mN/m at 20 °C	Measured
Adsorption/Desorption	log K_{oc} = 3.3 at 35 °C	Measured
Dissociation Constant	Not determined	Not expected as the chemical does not contain dissociable functionalities
Flash Point	144.5 °C at 101.3 kPa	Measured
Flammability	Not expected to be highly flammable	Estimated based on chemical structure
Autoignition Temperature	395 °C	Measured
Explosive Properties	Predicted negative	Estimated based on chemical structure
Oxidising Properties	Predicted negative	Estimated based on chemical structure

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 within Australia. The notified chemical will be imported into Australia as a component of fragrance formulations at ≤ 3.3% concentration.

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
Perth (by air)

IDENTITY OF RECIPIENTS
Givaudan Australia Pty Ltd

TRANSPORTATION AND PACKAGING
The notified chemical will be imported as a component of fragrance formulations at ≤ 3.3% concentration in glass, lacquer-lined containers of sizes ranging 1-190 kg. Finished consumer products containing ≤ 0.21% notified chemical will be transported primarily by road to retail stores in packages suitable for retail sale.

USE
The notified chemical will be used as a fragrance ingredient in cosmetic and household products (at ≤ 0.21% concentration in fine fragrances, at ≤ 0.15% concentration in other cosmetics and at ≤ 0.17% concentration in household products).

OPERATION DESCRIPTION
The notified chemical will be imported as a component of fragrance formulations at ≤ 3.3% concentration for reformulation into cosmetic and household products.

Reformulation
The procedures for reformulating the fragrance formulations containing the notified chemical will likely vary depending on the nature of the cosmetic/household products, and may involve both automated and manual transfer steps. In general, it is expected that the reformulation processes will involve blending operations that will normally be automated and occur in an enclosed system, followed by automated filling of the finished products into consumer containers of various sizes.

End-use
The finished products containing the notified chemical (at ≤ 0.21% concentration in fine fragrances, at ≤ 0.15% concentration in other cosmetics and at ≤ 0.17% concentration in household products) may be used by consumers and professionals such as hairdressers, workers in beauty salons or cleaners. Depending on the nature of the products, these could be applied in a number of ways, such as by hand, using an applicator or by spray.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and warehouse workers	unknown	unknown
Mixing	4	2
Drum handling	4	2
Drum cleaning/washing	4	2
Maintenance	4	2
Quality control	4	2
Packaging	4	2
Professional end users	not specified	not specified

EXPOSURE DETAILS

Transport and storage
Transport and storage workers may come in contact with the notified chemical either at ≤ 3.3% concentration in fragrance formulations or at ≤ 0.21% concentration in consumer products only in the event of an unlikely accidental rupture of containers.

Reformulation
During reformulation into consumer products, dermal, ocular and inhalation exposure of workers to the notified chemical at ≤ 3.3% concentration may occur. Exposure is expected to be minimised through the use of exhaust ventilation and/or automated/enclosed systems as well as through the use of personal protective equipment (PPE) such as coveralls, eye protection, impervious gloves and respiratory protection (as appropriate).

End use
Exposure to the notified chemical in end-use products at ≤ 0.21% concentration may occur in professions where the services provided involve the application of cosmetic products to clients (e.g. hair dressers, workers in beauty salons), 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 workers may use some PPE to minimise repeated exposure and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified chemical.

6.1.2. Public Exposure

There will be widespread and repeated exposure of the public to the notified chemical at ≤ 0.21% concentration through the use of cosmetic and household products. The principal 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 tables (SCCS, 2012; Cadby *et al.*, 2002; ACI, 2010; Loretz *et al.,* 2006). For the purposes of the exposure assessment, Australian use patterns for the various product categories are assumed to be similar to those in Europe. A dermal absorption (DA) of 100% was assumed for the notified chemical for calculation purposes. For the inhalation exposure assessment, a 2-zone approach was used (Steiling *et al*., 2014; Rothe *et al*., 2011; Earnest, Jr, 2009). An adult inhalation rate of 20 m^3/day (enHealth, 2012) was used and it was conservatively assumed that the fraction of the notified chemical inhaled is 50%. 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)	C (%)	Retention Factor (RF) (unitless)	Daily systemic exposure (mg/kg bw/day)
Body lotion	7820	0.15	1	0.1833
Face cream	1540	0.15	1	0.0361
Hand cream	2160	0.15	1	0.0506
Fine fragrances	750	0.21	1	0.0246
Deodorant spray	1430	0.15	1	0.0352
Shampoo	10460	0.15	0.01	0.0025
Conditioner	3920	0.15	0.01	0.0009
Shower gel	18670	0.15	0.01	0.0044
Hand wash soap	20000	0.15	0.01	0.0047
Hair styling products	4000	0.15	0.1	0.0094
Total				0.3516

C = concentration of the notified chemical; RF = retention factor.
Daily systemic exposure = (Amount × C × RF × DA)/BW

Household Products (Indirect dermal exposure – from wearing clothes)

Product type	Amount (g/use)	C (%)	Product Retained (PR) (%)	Percent Transfer (PT) (%)	Daily systemic exposure (mg/kg bw/day)
Laundry liquid	230	0.17	0.95	10	0.0056
Fabric softener	90	0.17	0.95	10	0.0022
Total					0.0078

Daily systemic exposure = (Amount × C × PR × PT × DA)/BW

Household products (Direct dermal exposure)

Product type	Frequency (use/day)	C (%)	Contact Area (cm^2)	Product Usage (g/cm^3)	Film Thickness (cm)	Time Scale Factor (unitless)	Daily systemic exposure (mg/kg bw/day)
Laundry liquid	1.43	0.17	1980	0.01	0.01	0.007	0.0001
Dishwashing liquid	3	0.17	1980	0.009	0.01	0.03	0.0004
All-purpose cleaner	1	0.17	1980	1	0.01	0.007	0.0036
Total							0.0040

Daily systemic exposure = (Frequency × C × Contact Area × Product Usage × Film Thickness on skin × Time Scale Factor × DA)/BW

Aerosol products (Inhalation exposure)

Product type	Amount	C	Inhalation Rate	Exposure Duration (Zone 1)	Exposure Duration (Zone2)	Fraction Inhaled	Volume (Zone 1)	Volume (Zone 2)	Daily systemic exposure
	(g/day)	(%)	(m^3/day)	(min)	(min)	(%)	(m^3)	(m^3)	(mg/kg bw/day)
Hairspray	9.89	0.15	20	1	20	50	1	10	0.0048

Daily systemic exposure = [(Amount × C × Inhalation Rate × Fraction Inhaled × 0.1) / BW × 1440)] × [Exposure Duration (Zone 1)/Volume (Zone 1) + Exposure Duration (Zone 2)/Volume (Zone 2)]

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above tables that contain the notified chemical. This would result in a combined internal dose of 0.3682 mg/kg bw/day. It is acknowledged that inhalation exposure to the notified chemical from use of other cosmetic and household products (in addition to hair spray) may occur. However, it is considered that the combination of the conservative (screening level) hair spray inhalation exposure assessment parameters, and the aggregate exposure from use of the dermally applied products, which assumes a conservative 100% absorption rate, is sufficiently protective to cover additional inhalation exposure to the notified chemical from use of other spray cosmetic and household products with lower exposure factors (e.g., air fresheners).

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
Skin irritation (*in vitro*)	irritating
Eye irritation (*in vitro*)	non-irritating
Mouse, skin sensitisation – Local lymph node assay	evidence of sensitisation (EC_3 = 25%)
Rat, repeat dose oral toxicity – 28 days	NOAEL = 150 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics

Based on the low molecular weight (< 500 Da), water solubility (2.45 × 10^{-2} g/L at 20 °C) and partition coefficient (log Pow = 3.7 at 35 °C) of the notified chemical, there is potential for the chemical to cross biological membranes.

Acute toxicity

The notified chemical was found to be of low toxicity via the oral route in a study conducted in rats.

Irritation

In an *in vitro* skin irritation study conducted using the reconstructed human epidermis model (EpiSkin™), the notified chemical was determined to be irritating to the skin. In an *in vitro* bovine corneal opacity and permeability (BCOP) test the notified chemical was determined to be non-irritating to eyes.

Sensitisation

The notified chemical was a skin sensitiser in mice (local lymph node assay: stimulation indices were 3.0, 7.5 and 8.8 at 25%, 50% and 100%, respectively). The EC_3 value was calculated to be 25%.

Repeated dose toxicity

A repeated dose oral (gavage) toxicity study on the notified chemical was conducted in rats, in which the test substance was administered at 50, 150 and 500 mg/kg bw/day for 28 consecutive days, with a 14-day recovery period for high dose and control animals.

The No Observed Adverse Effect Level (NOAEL) was established as 150 mg/kg bw/day in this study based on morphological changes in the liver of males and females (hepatocellular hypertrophy combined with a weight increase of over 25%), and in the kidney of males (hyaline droplet accumulation with tubular degeneration/regeneration), in the high dose group. However the findings in the kidney are not considered to be relevant to humans.

Mutagenicity/Genotoxicity

The notified chemical was negative in a bacterial reverse mutation assay.

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*
Skin Irritation (Category 2)	H315 - Causes skin irritation
Skin Sensitisation (Category 1)	H317 - May cause sensitization by skin contact

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):

R38: Irritating to skin
R43: May cause sensitisation by skin contact

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on the available toxicological information and use pattern, the critical health effects of the notified chemical are as a skin irritant and skin sensitiser. Adverse effects could also occur after repeated exposure.

Reformulation
During reformulation, workers may be at risk of sensitisation effects when handling the notified chemical at ≤ 3.3% concentration. It is anticipated by the notifier that engineering controls such as enclosed and automated processes and local ventilation will be implemented where possible, and appropriate PPE (coveralls, imperious gloves, eye protection and respiratory protection) will be used to limit worker exposure.

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.

End-use
Workers involved in professions where the services provided involve the application of cosmetic and household products containing the notified chemical to clients (*e.g.*, hairdressers, beauty salon workers and cleaners) may be exposed to the notified chemical at concentrations up to 0.21%. Such professionals may use PPE 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 experienced by consumers using the various products containing the notified chemical.

6.3.2. Public Health
Cosmetic and household products containing the notified chemical at ≤ 0.21% concentration will be available to the public. The main route of exposure is expected to be dermal and inhalation, with some potential for accidental ocular or oral exposure.

Irritation
The notified chemical is a skin irritant. However, skin irritation effects are not expected from use of the notified chemical at the proposed low concentrations in cosmetic and household products.

Sensitisation
When tested in an LLNA study, the notified chemical was considered as a skin sensitiser. Proposed methods for the quantitative risk assessment of the dermal sensitisation have been the subject of significant discussion (i.e., Api *et al.,* 2008 and RIVM, 2010). Using fine fragrance as an example for products that may contain the notified chemical (at ≤ 0.21% concentration), as a worst case scenario, the Consumer Exposure Level (CEL) is estimated to be 7.88 μg/cm^2/day (Cadby *et al.,* 2002). Consideration of available information and application of appropriate safety factors allowed the derivation of an Acceptable Exposure Level (AEL) of 19.75 μg/cm^2/day. In this instance, the factors employed included an interspecies factor (3), intraspecies factor (10), a matrix factor (3.16), use/time factor (3.16) and database factor (1), giving an overall safety factor of 300.

As the AEL > CEL, the risk to the public of the induction of sensitisation that is associated with the use of fine fragrances (a worst case example of a leave-on cosmetic product) is not considered to be unreasonable. Based on lower expected exposure level from other cosmetic products and household products, by inference, the risk of induction of sensitisation associated with the use of these products is also not considered to be unreasonable. However, it is acknowledged that consumers may be exposed to multiple products containing the notified chemical, and a quantitative assessment based on aggregate exposure has not been conducted.

Repeated dose toxicity
The repeated dose toxicity potential was estimated by calculation of the margin of exposure (MoE) of the notified chemical using the worst case exposure scenario from use of multiple products of 0.3682 mg/kg bw/day (see Section 6.1.2). Using a NOAEL of 150 mg/kg bw/day derived from a 28 day repeated dose oral toxicity study on the notified chemical, the margin of exposure (MoE) was estimated to be 407. A MOE value ≥ 100 is generally considered to be acceptable for taking into account intra- and inter-species differences. Therefore, the MoE is considered to be acceptable.

Therefore, the risk to the public from use of the notified chemical at ≤ 0.21% in fine fragrances, ≤ 0.15% in other cosmetics and ≤ 0.17% in 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 a component of fragrance formulations, for reformulation into finished cosmetic and household products. There is unlikely to be any significant release to the environment from transport and storage, except in the case of accidental spills and leaks. Leaks and spills of the product containing the notified chemical is expected to be collected and disposed of to landfill in accordance with local government regulations.

The reformulation process will involve blending operations that will occur within a fully enclosed system. Therefore, significant release of the notified chemical from this process to the environment is not expected. Wastes containing the notified chemical generated from reformulation include equipment wash water, empty import containers and spilt materials (< 1% of the total import volume as indicated by the notifier) are expected to be disposed of to on-site waste water treatment or directly to sewer system. Empty import containers 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 compartments through sewers during its use in various cosmetic formulations and household products.

RELEASE OF CHEMICAL FROM DISPOSAL
It is estimated by the notifier that a maximum of 1% of the import volume of the notified chemical may remain in end-use containers once the consumer products are used up. Wastes and residue of the notified chemical in empty 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
The chemical is not readily biodegradable (0% biodegradation in 28 days and 44% in 60 days). However, the chemical is inherently biodegradable based on the results from an inherent biodegradability study (77% biodegradation in 60 days). For details of the environmental fate study, please refer to Appendix C.

Following its use in cosmetic formulations and household products in Australia, the majority of the notified chemical will enter into the sewer system before potential release to surface waters nationwide. The notified chemical is expected to partially adsorb to sediment or any suspended particulate matter based on the soil/water adsorption coefficient (log Koc = 3.3) and low water solubility. A small proportion of the notified chemical may be applied to land when effluent is used for irrigation, when sewage sludge is used for soil remediation. The notified chemical may also be applied to land when disposed of to landfill as collected spills and empty container

residue. The notified chemical residues in landfill, soil and sediment are expected to eventually degrade through biotic and abiotic processes to form water and oxides of carbon.

The notified chemical may have a potential to bioaccumulate in aquatic life based on its relatively high log Pow (log Pow = 3.7). However, significant bioaccumulation is not expected as the notified chemical is inherently biodegradable.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated assuming that 100% release of the notified chemical into sewer systems nationwide through sewage treatment plants (STPs) and there is no removal of the notified chemical at 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:	0.61	µg/L
PEC - Ocean:	0.06	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.61 µg/L may potentially result in a soil concentration of approximately 4.04 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 20.19 µg/kg and 40.39 µg/kg, respectively.

7.2. Environmental Effects Assessment

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 = 1.09 mg/L	Toxic to fish
Daphnia Toxicity	48 h EC50 = 1.01 mg/L	Toxic to aquatic invertebrates
Algae Toxicity	72 h EC50 = 1.55 mg/L	Toxic to algae
Inhibition of Bacterial Respiration	3 h EC50 > 100 mg/L	Not inhibitory to microbial respiration

Based on the above ecotoxicological endpoints for the notified chemical, it is considered 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 the acute toxicity and not ready biodegradability of the notified chemical, it is formally classified as “Chronic Category 2; Toxic to aquatic life” under the GHS for chronic toxicity.

7.2.1. Predicted No-Effect Concentration

The predicted no-effects concentration (PNEC) has been calculated from the most sensitive endpoint for daphnia. An assessment factor of 100 was used given measured acute endpoints from three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment	
EC50 (Daphnia, 48 h)	1.01 mg/L
Assessment Factor	100
PNEC:	10.1µg/L

7.3. Environmental Risk Assessment

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.61	10.1	**0.06**
Q - Ocean	0.06	10.1	**0.006**

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 use volume and assessed use pattern. Although the notified chemical may have potential to bioaccumulate in aquatic life, this is expected to be mitigated as the notified chemical is inherently biodegradable.

On the basis of the PEC/PNEC ratio, maximum annual importation volume 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/Freezing Point < -50 °C

Method OECD TG 102 Melting Point/Melting Range.
Remarks Determined using a crystallising apparatus.
Test Facility Givaudan (2015a)

Boiling Point 284 °C at 101.3 kPa

Method OECD TG 103 Boiling Point.
Remarks Siwoloboff Method
Test Facility Givaudan (2015b)

Density 948 kg/m^3 at 20 °C

Method OECD TG 109 Density of Liquids and Solids.
Remarks Oscillating densitimeter method
Test Facility Givaudan (2015c)

Vapour Pressure 1×10^{-4} kPa at 20 °C

Method OECD TG 104 Vapour Pressure.
Remarks Gas saturation method
Test Facility Givaudan (2015d)

Water Solubility 2.45×10^{-2} g/L at 20 °C

Method OECD TG 105 Water Solubility.
Remarks Flask Method
Test Facility Givaudan (2015e)

Hydrolysis as a Function of pH

Method OECD TG 111 Hydrolysis as a Function of pH.

pH	*T (°C)*	*$t_{½}$ <days>*
4	25	> 365
7	25	> 365
9	25	131.7

Remarks At pH 9.0, the test substance concentration decreased at 50 °C and 60 °C and the decrease is faster at 50 °C than that at 60 °C. Given the test substance does not contain any hydrolysable groups, this concentration reduce is considered to be due to other dissipation pathway such as biodegradation. The half life at pH 9 was calculated to be 131.7 days by assuming that the concentration reduction at pH 9.0 is solely due to hydrolysis.
Test Facility Givaudan (2015f)

Partition Coefficient (n-octanol/water) log Pow = 3.7 at 35 °C

Method OECD TG 117 Partition Coefficient (n-octanol/water).
Remarks HPLC Method
Test Facility Givaudan (2015g)

Surface Tension 45.9 mN/m at 20 °C

Method OECD TG 115 Surface Tension of Aqueous Solutions.
Remarks Concentration: ~90% of the saturation concentration.
Test Facility Givaudan (2015h)

Adsorption/Desorption – screening test

log K_{oc} = 3.3 at 35 °C

Method	OECD TG 121 Estimation of the Adsorption Coefficient (Koc) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC).
Remarks	Reverse High Performance Liquid Chromatography method
Test Facility	Givaudan (2015i)

Flash Point

144.5 °C at 101.3 kPa

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

Autoignition Temperature

395 ± 10 °C

Method	DIN 51794
Remarks	Determined in a SUR BERLIN oven
Test Facility	Givaudan (2015k)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 420 Acute Oral Toxicity – Fixed Dose Procedure.
Species/Strain	Rat/Wistar
Vehicle	None
Remarks - Method	No significant protocol deviations. A pilot study was conducted in a female animal at a dose of 2000 mg/kg bw. The dose was selected for the main study based on the results of the pilot study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	1F	2000	0/1
2	4F	2000	0/4

LD50	> 2000 mg/kg bw
Signs of Toxicity	Signs of systemic toxicity including hunched posture, uncoordinated movements and/or piloerection were noted on Day 1.
Effects in Organs	No abnormalities were noted at macroscopic examination.
Remarks - Results	The animals showed expected body weight gain over the observation period.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	WIL (2015a)

B.2. Irritation – skin (in vitro)

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 439 In vitro Skin Irritation: Reconstructed Human *Epidermis* Test Method EPISKIN-SM™ Reconstructed Human Epidermis Model
Vehicle	None
Remarks - Method	In a preliminary test the test substance was shown to directly reduce MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolim bromide]. Therefore, the study was performed in parallel on viable and water-killed tissues. The test substance (25 µL) was applied to the tissues in triplicate. Following exposure periods of 15 ± 0.5 minutes (room temperature), the tissues were rinsed, treated with MTT and then incubated at 37 °C for 42 hours. Negative and positive controls were run in parallel with the test substance: - Negative control: phosphate buffered saline (PBS) - Positive control: 5% sodium dodecyl sulphate in PBS

RESULTS

Test material	*Mean OD_{570} of triplicate tissues*	*Relative mean Viability (%)*	*SD of relative mean viability*
Negative control	0.957	100	< 6%
Test substance	0.310	32	< 6%
Positive control	0.226	24	< 6%

OD = optical density; SD = standard deviation

Remarks - Results	The results from the additional procedure using water-killed tissues showed the non–specific reduction of MTT by the test substance was 3% of the negative control tissues. The net OD of the water-killed tissues was subtracted from the ODs of the test substance treated viable tissues. The relative mean viability of the tissues treated with the test substance was 32% (predicted as irritating according to the criteria as below 50%). The positive and negative controls gave satisfactory results, confirming the validities of the test systems.
CONCLUSION	The notified chemical was considered irritating to the skin under the conditions of the test.
TEST FACILITY	WIL (2015b)

B.3. 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
Vehicle	None
Remarks - Method	No significant protocol deviations. The positive control was 10% benzalkonium chloride in physiological saline.

RESULTS

Test material	*Mean opacities of triplicate tissues (SD)*	*Mean permeabilities of triplicate tissues (SD)*	*IVIS (SD)*
Vehicle control	0.0	0.000	0.0
*Test substance**	1.3	0.022	1.7
*Positive control**	103.0	3.287	152.3

SD = Standard deviation; IVIS = in vitro irritancy score
*Corrected for background values

Remarks - Results	The in vitro irritancy score (IVIS) value for the test substance was lower than the cut-off value for GHS no category (≤ 3). The positive and negative controls gave satisfactory results, confirming the validities of the test systems.
CONCLUSION	The notified chemical was considered non-irritating to the eye under the conditions of the test.
TEST FACILITY	WIL (2015c)

B.4. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
Species/Strain	Mouse/CBA/J
Vehicle	Acetone/olive oil (4:1)
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 No significant protocol deviations

RESULTS

Concentration (% w/w)	*Number and sex of animals*	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance			
0 (vehicle control)	5F	505 ± 84	-
25%	5F	1504 ± 245	3.0
50%	5F	3792 ± 741	7.5
100%	5F	4436 ± 408	8.8

EC3 25%

Remarks - Results In the preliminary study, there were no signs of systemic toxicity or irritation (the latter was indicated by < 25% increase in mean ear thickness) noted.

In the main study, there were no mortality or signs of systemic toxicity observed in the test or control animals. Very slight irritation was noted on the ears of animals treated with the test substance at 50% and 100% concentrations on Days 3 and/or 4. Scaliness was noted for the animals treated at 100% concentration on Day 6.

The auricular lymph nodes of the animals in control and 25% concentration groups were considered normal in size while the nodes of the animals in 50% and 100% concentration groups were considered enlarged. No macroscopic abnormalities of the surrounding area were noted for any animals.

The test substance elicited a SI ≥ 3 and is therefore considered a skin sensitiser.

All treated animals showed body weight changes comparable to those of the vehicle control group.

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

TEST FACILITY WIL (2015d)

B.5. 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
Post-exposure observation period: 14 days

Vehicle Corn oil

Remarks - Method No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5 per sex	0	0/10
low dose	5 per sex	50	0/10

mid dose	5 per sex	150	0/10
high dose	5 per sex	500	0/10
control recovery	5 per sex	0	0/10
high dose recovery	5 per sex	500	0/10

Mortality and Time to Death
There were no unscheduled deaths.

Clinical Observations
No clinical signs of systemic toxicity were noted. There were no changes in hearing ability, pupillary reflex and static righting and grip strength. Motor activities were lower in both female and male animals treated with 500 mg/kg/day at the end of the treatment period but appeared normal after the 14-day recovery period. These changes were not considered by the study authors to represent an adverse effect on neurobehaviour as they were not supported by any other clinical signs or abnormalities during functional observations or morphological changes in neuronal tissues.

Slightly reduced body weight gain and lower body weight noted in male animals treated with 500 mg/kg/day was not considered by the study authors to be adverse as the changes were slight.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Increase incidence and severity of hyaline droplet accumulation was noted in the kidney of male animals treated with 500 mg/kg/day. This change was considered by the study authors to likely represent alpha 2u-globulin, a male rat specific protein which is not present in female rats or human. This finding was accompanied by minimal to slight tubular degeneration/regeneration and was therefore considered by the study authors to be adverse.

A slightly higher creatinine and potassium level and lower chloride level were also noted and their relation to treatment could not be ruled out.

Higher alanine aminotransferase and alkaline phosphatase activity, higher total bilirubin, albumin, bile acids and lower cholesterol noted in male and/or female animals treated with 500 mg/kg/day could be related to hepatocellular hypertrophy noted in the liver.

Effects in Organs
Hepatocellular hypertrophy in the liver combined with a weight increase of over 25% was noted in male and female animals treated with 500 mg/kg/day and partially recovered in male animals and completely recovered in female animals. Minimal hepatocellular hypertrophy noted in 1 male animal treated with 150 mg/kg/day in absence of significant liver weight changes and any degeneration changes was not considered by the study authors to be adverse.

Slightly increased incidence and severity of follicular cell hypertrophy noted in the thyroid gland in both sexes treated with 500 mg/kg/day with complete recovery after 14-day recovery period was considered by the study authors to be an adaptive change and non-adverse.

Remarks – Results
Slight changes in haematology parameters were considered by the study authors to suggest an effect on red blood cell metabolism and to be non-adverse.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 150 mg/kg bw/day in this study, based on morphological changes in the liver of male and female animals, and in the kidney of male animals.

TEST FACILITY WIL (2015e)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

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

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	S9 mix from Aroclor 1254 induced rat liver
Concentration Range in Main Test	Test 1 a) With metabolic activation: 5.4-5000 µg/plate b) Without metabolic activation: 5.4-5000 µg/plate Test 2 a) With metabolic activation: 0.54-5000 µg/plate b) Without metabolic activation: 1.7-5000 µg/plate Test 3 a) Without metabolic activation: 0.54-1600 µg/plate
Vehicle	Dimethyl sulfoxide
Remarks - Method	Test 1 was carried out at 5.4-5000 µg/mL. The dose selection for Test 2 was based on the toxicity observed in Test 1. Based on the results of Test 2, Test 3 was carried out at 0.54-1600 µg/mL using TA98 only in the absence of metabolic activation. Positive controls: With metabolic activation: 2-aminoanthracene Without metabolic activation: sodium azide (TA1535); methyl methanesulfonate (TA100); ICR-191 (TA1537); 2-nitrofluorene (TA98)

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*		
	Cytotoxicity in Main Test	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 52	> 512	negative
Test 2	> 17	> 512	negative
Test 3 (TA98)	> 164	> 512	negative
Present			
Test 1	> 52	> 512	negative
Test 2	> 164	> 512	negative

Remarks - Results	No significant increases in the frequency of revertant colonies were observed for any of the bacterial strains, with any dose of the test substance, either with or without metabolic activation. The positive and negative controls gave a satisfactory response confirming the validity of the test system.

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

TEST FACILITY WIL (2015f)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Activated sludge
Exposure Period	60 days
Auxiliary Solvent	None
Analytical Monitoring	Oxygen consumption
Remarks - Method	Conducted in accordance with the test guidelines above, and in compliance with GLP standards and principles. Toxicity control was not conducted in parallel. However, this is not considered to affect the validity of the study because the test substance was determined to not have significantly adverse effects on bacterial respiration in the following bacterial respiration study.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
14	0	14	82
28	0	21	86
42	11	28	87
60	44	60	90

Remarks - Results	The oxygen consumption was reduced in the test media compared to the sludge only control during some days of the test. However, the results are considered to be reliable as the test substance did not significantly inhibit the intrinsic respiration of the inoculums.
CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	Givaudan (2015l)

C.1.2. Inherent biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 302C Inherent Biodegradability: Modified MITI test
Inoculum	Activated sludge
Exposure Period	60 days
Auxiliary Solvent	None
Analytical Monitoring	Oxygen consumption
Remarks – Method	The test was conducted according to the test guideline above without significant deviation from the protocol.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*

14	0	5	66
28	0	7	72
35	11	14	82
42	44	21	86
49	65	28	87
56	75	60	90
60	77		

Remarks – Results: All validity criteria are satisfied. The test substance does not inhibit the intrinsic respiration of the inoculum at the test concentration.

CONCLUSION: The notified chemical is inherently biodegradable.

TEST FACILITY: Givaudan (2015m)

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: *Danio rerio*

Exposure Period: 96 hours

Auxiliary Solvent: Acetone

Water Hardness: ~ 200 mg $CaCO_3$/L

Analytical Monitoring: GC-MS

Remarks – Method: The study was conducted according to the above guideline without significant deviation from the protocol.

The test media were renewed every 24 hours.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*6 h*	*24 h*	*48 h*	*72 h*	*96 h*
Solvent Control	-	7	0	0	0	1	1
0.48		7	0	1	2	2	2
0.86		7	0	0	0	0	1
1.54		7	0	0	0	1	2
2.78		7	0	3	3	6	6
5.0		7	0	6	7	7	7

LC50: 1.09 mg/L at 96 hours (95% confidence limit: 0.546 - 1.72 mg/L)

Remarks – Results: All validity criteria were satisfied.

At the nominal concentration of 0.86 mg/L, 1 fish was found to have reduced swimming after 6 hours exposure and 1 fish showed hanging posterior fin after 48 hours exposure.

At the nominal concentration 1.54 mg/L, 7 fishes were found to have reduced swimming and 3 fishes showed hanging posterior fin after 3 hours exposure.

The measured concentrations of the test substances were not in the range of 80-120% of the nominal concentrations due to the degradation of the test degrade during the test. The results are considered to be reliable as the test results are based on mean measured concentrations.

CONCLUSION	The notified chemical is toxic to fish.
TEST FACILITY	Givaudan (2015n)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test - Semi-static
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	Acetone
Water Hardness	254 mg $CaCO_3$/L
Analytical Monitoring	GC-MS
Remarks - Method	The test was conducted according to the above test guideline without significant deviation from the protocol. The water hardness of the test media is slightly higher than the recommended values between 140 and 250 mg/L. This negligible water hardness difference is not considered to significantly affect the toxic effects of the test substance on daphnia. The test was conducted under semi-static condition with the test solutions renewed every 24 hours.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Control	-	20	2	2
0.476	0.298	20	0	0
0.857	0.621	20	0	1
1.54	1.09	20	1	12
2.78	2.97	20	16	20
5.0	5.67	20	20	20

EC50	1.01 mg/L at 48 hours (95% confidence limit: 0.874-1.25mg/L)
Remarks - Results	All validity criteria were satisfied. At the test concentration 0.476 mg/L, 1 daphnid was lying at vessel bottom after 48 hours exposure. At the test concentration 0.857 mg/L, 2 daphnids showed reduced swimming activity after 48 hours exposure. At the test concentration 1.54 mg/L, 2 daphnids were lying at vessel bottom after 24 hour exposure, 1 daphnids were lying at vessel bottom and 1 daphnids showed reduced swimming activity after 48 hours exposure. At the test concentration 2.78 mg/L, 4 daphnids showed reduced swimming activity after 24 hour exposure to the test substance. The measured concentrations of the test substances were not in the range of 80-120% of the nominal concentrations due to the degradation of the test degrade during the test. The test results are based on mean measured concentrations.
Conclusion	The notified chemical is toxic to the invertebrates.
Test Facility	Givaudan (2015o)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test - Static.
Species	*Desmodesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: Solvent control, 0.21, 0.47, 1.03, 2.27 and 5.00 mg/L Actual: NA, 0.198, 0.407, 0.834, 2.31 and 5.33 mg/L
Auxiliary Solvent	Acetone
Water Hardness	Not available
Analytical Monitoring	GC-MS
Remarks - Method	The study was conducted according to the above guideline without significant deviation from the protocol.

RESULTS

Biomass		*Growth*	
EC50 *mg/L at 72 h*	*NOEC* *mg/L*	*EC50* *mg/L at 72 h*	*NOEC* *mg/L*
0.719 (95% confident limit: 0.675-0.766)	0.123	1.55 (95% confident limit:1.47 – 1.62)	0.123

Remarks - Results	All validity criteria were satisfied. A distinct concentration decrease was observed throughout the test due to the degradation of the test substance. The test results are based on mean measured concentrations.
CONCLUSION	The notified chemical is toxic to algae.
TEST FACILITY	Givaudan (2015p)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum	Activated sludge
Exposure Period	3 hours
Concentration Range	Nominal: 100 mg/L Actual: not determined
Remarks – Method	One limit test concentration of 100 mg/L was tested during the study. No significant deviations from the test guidelines above were reported.
RESULTS	
EC50	> 100 mg/L
Remarks – Results	The actual concentration of the test substance was not determined and the result was based on nominal concentration.
CONCLUSION	The notified chemical is not inhibitory to bacterial respiration.
TEST FACILITY	Givaudan (2015q)

BIBLIOGRAPHY

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

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

Earnest, C.W., Jr. (2009) A Two-Zone Model to Predict Inhalation Exposure to Toxic Chemicals in Cleaning Products, MScEng thesis, The University of Texas at Austin.

enHealth (2012) Australian Exposure Factor Guide, companion document to: Environmental Health Risk Assessment: Guidelines for assessing human health risks from environmental hazards, EnHealth, Commonwealth of Australia.

Givaudan (2015a) Freezing Point of GR-88-0778 (Study No. 14-E196, March, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2015b) Boiling Point of GR-88-0778 (Study No. 14-E197, March, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2015c) Density of GR-88-0778 (Study No. 14-E201, June, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2015d) Vapour Pressure of GR-88-0778 (Study No. 14-E194, April, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2015e) Water solubility of GR-88-0778 (Study No. 14-E198, June, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2015f) Hydrolysis as a function of pH of GR-88-0778 (Study No. 14-E206, December, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2015g) Partition coefficient n-octanol/water of GR-88-0778 (Study No. 14-E193, June, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2015h) Surface Tension of an Aqueous Solution of GR-88-0778 (Study No. 14-E199, June, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2015i) Adsorption coefficient (K_{oc}) of GR-88-0778 (Study No. 14-E200, June, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2015j) Flash Point of GR-88-0778 (Study No. 14-E195, February, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2015k) Auto-ignition Temperature of GR-88-0778 (Study No. 2015-293, May, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2015l) Ready biodegradability of GR-88-0778 (Study No. 14-E205, September, 2015). Geneva, Switzerland, Givaudan International SA (Unpublished report submitted by the notifier).

Givaudan (2015m) Inherent biodegradability of GR-88-0778 (Study No. 15-E103, September, 2015). Geneva, Switzerland, Givaudan International SA (Unpublished report submitted by the notifier).

Givaudan (2015n) GR-88-0778: A study on the Acute Toxicity to Zebrafish (*Danio rerio*) (Study No. 15BZ1FY, October, 2015). Geneva, Switzerland, Givaudan International SA (Unpublished report submitted by the notifier).

Givaudan (2015o) GR-88-0778: A study on the Acute Toxicity to Daphnia magna (Study No. 15BZ3DA, October, 2015). Geneva, Switzerland, Givaudan International SA (Unpublished report submitted by the notifier).

Givaudan (2015p) GR-88-0778: A study on the Toxicity to Algae (*Desmodesmus subspicatus*) (Study No. 15BZ4AO, October, 2015). Geneva, Switzerland, Givaudan International SA (Unpublished report submitted by the notifier).

Givaudan (2015q) Activated sludge respiration inhibition test with GR-88-0778 (Study No. 15-E186, October, 2015). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

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. (2006) Exposure data for personal care products : Hairspray, spray perfume, liquid foundation, shampoo, body wash, and solid antiperspirant, Food and Chemcial Toxicology 44:2008-2018.

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

RIVM (2010) Observations on the Methodology for Quantitative Risk Assessment of Dermal Allergens, Report 320015003/2010, National Institute for Public Health and the Environment.

Rothe, H., Fautz, R., Gerber, E., Neumann, L., Rettinger, K., Schuh, W., Gronewold, C. (2011) Special aspects of cosmetic spray evaluations: Principles on inhalation risk assessment, Toxicology Letters 205 (2011) 97-104.

SCCS (2012) Notes of Guidance for testing of Cosmetic Ingredients and Their Safety Evaluation (7th revision) European Commission - Scientific Committee on Consumer Safety.

Steiling, W., Bascompta, M., Carthew, P., Catalano, G., Corea, N., D'Haese, A., Jackson, P., Kromidas, L., Meurice, P., Rothe, H., Singal, M. (2014) Principle considerations for the risk assessment of sprayed consumer products, Toxicology Letters 227:41-49.

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 (2015a) Assessment of Acute Oral Toxicity with GR-88-0778 in the Rat (Fixed Dose Method) (Project No. 508331, April, 2015). S'-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2015b) In Vitro Skin Irritation Test with GR-88-0778 Using a Human Skin Model (Project No. 508332, July, 2015). S'-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2015c) Evaluation of the Eye Hazard Potential of GR-88-0778 Using the Bovine Corneal Opacity and Permeability Test (BCOP Test) (Project No. 508333, April, 2015). S'-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2015d) Assessment of Contact Hypersensitivity to GR-88-0778 in the Mouse (Local Lymph Node Assay) (Project No. 508334, July, 2015). S'-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2015e) Repeated Dose 28-Day Toxicity Study with GR-88-0778 by Daily Gavage in the Rat Followed by a 14-Day Recovery Period (Project No. 508337, September, 2015). S'-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).

WIL (2015f) Evaluation of the Mutagenic Activity of GR-88-0778 in the *Salmonella Typhimurium* Reverse Mutation Assay and the *Escherichia Coli* Reverse Mutation Assay (Project No. 508335, May, 2015). S'-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by the notifier).