File No: LTD/1924

March 2017

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

1*H*-Inden-1-one, 2,3-dihydro-2,3,3-trimethyl-

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/1924	Givaudan Singapore Pte Ltd	1*H*-Inden-1-one, 2,3-dihydro-2,3,3-trimethyl-	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

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:

R38: Irritation to skin

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.

Based on the available information, when used at ≤ 0.5% concentration in fine fragrances, at ≤ 0.1% concentration in other cosmetics or at ≤ 0.07% 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 reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Skin irritation (Category 2): H315 – Causes skin irritation

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

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical during reformulation:
  - Avoid contact with skin

  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 physical containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical 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 0.5% in fine fragrances, 0.1% in other cosmetics, or 0.07% 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 (2004), Switzerland (2004), USA (2005) and China (2007)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Safraleine

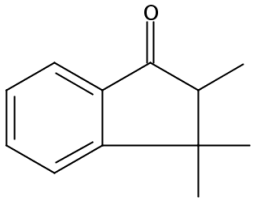
CAS NUMBER
54440-17-4

CHEMICAL NAME
1*H*-Inden-1-one, 2,3-dihydro-2,3,3-trimethyl-

OTHER NAME(S)
GR-85-4441

MOLECULAR FORMULA
$C_{12}H_{14}O$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
174.24 Da

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

3. COMPOSITION

DEGREE OF PURITY
> 96%

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	251 °C at 101.3 kPa	Measured
Density	1,022 kg/m^3 at 20 °C	Measured
Vapour Pressure	1.2 × 10^{-3} kPa at 20 °C	Measured
Water Solubility	0.446 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionalities.
Partition Coefficient (n-octanol/water)	Log P_{OW} = 2.9	Measured
Adsorption/Desorption	Log K_{OC} = 2.725	Calculated based on partition coefficient using KOCWIN v2.00 (US EPA, 2011)
Dissociation Constant	Not determined	Contains no dissociable functionalities.
Flash Point	120 °C at 101.3 kPa	Measured
Flammability	Not expected to be highly flammable	Estimated based on chemical structure
Autoignition Temperature	Not determined	Not expected to undergo autoignition
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 ≤ 6.7% 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 ≤ 6.7% concentration in glass, lacquer-lined containers of sizes ranging 1-190 kg. Finished consumer products containing ≤ 0.5% 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 ≤ 0.5% concentration in fine fragrances, at ≤ 0.1% concentration in other cosmetics and at ≤ 0.07% concentration in household products).

OPERATION DESCRIPTION
The notified chemical will be imported as a component of fragrance formulations at ≤ 6.7% 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 ≤ 0.5% concentration in fine fragrances, at ≤ 0.1% concentration in other cosmetics and at ≤ 0.07% 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 ≤ 6.7% concentration in fragrance formulations or at ≤ 0.5% 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 ≤ 6.7% 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 ≤ 0.5% 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 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 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 ≤ 0.5% 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	0.1	1	0.1222
Face cream	1540	0.1	1	0.0241
Hand cream	2160	0.1	1	0.0338
Fine fragrances	750	0.5	1	0.0586
Deodorant spray	1430	0.1	1	0.0234
Shampoo	10460	0.1	0.01	0.0016
Conditioner	3920	0.1	0.01	0.0006
Shower gel	18670	0.1	0.01	0.0029
Hand wash soap	20000	0.1	0.01	0.0031
Hair styling products	4000	0.1	0.1	0.0063
Total				0.2766

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	0.07	0.95	10	0.0024
Fabric softener	90	0.07	0.95	10	0.0009
Total					0.0033

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	0.07	1980	0.01	0.01	0.007	0.0000
Dishwashing liquid	3	0.07	1980	0.009	0.01	0.03	0.0002
All-purpose cleaner	1	0.07	1980	1	0.01	0.007	0.0015
Total							0.0017

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 (g/day)	C (%)	Inhalation Rate (m^3/day)	Exposure Duration (Zone 1) (min)	Exposure Duration (Zone2) (min)	Fraction Inhaled (%)	Volume (Zone 1) (m^3)	Volume (Zone 2) (m^3)	Daily systemic exposure (mg/kg bw/day)
Hairspray	9.89	0.1	20	1	20	50	1	10	0.0032

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 0.2848 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
Rat, acute dermal toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rabbit, skin irritation	irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – local lymph node assay	no evidence of sensitisation
Human, skin sensitisation – RIPT (10%)	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days	NOAEL = 450 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* chromosome aberration test	genotoxic
Genotoxicity – *in vivo* mammalian erythrocyte micronucleus test	non-genotoxic

Toxicokinetics

Based on the low molecular weight (< 500 Da), water solubility (4.46×10^{-2} g/L at 20 °C) and partition coefficient (log Pow = 2.9 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 and dermal routes in studies conducted in rats.

Irritation

In studies conducted in rabbits, the notified chemical was found to be irritating to the skin and slightly irritating to eyes. Eye irritation was limited to slight to moderate conjunctival irritation which was fully resolved 48 hours after treatment.

Sensitisation
The notified chemical was not a skin sensitiser in mice when tested at up to 100% concentration in a local lymph node assay. In a human repeat insult patch test (HRIPT), a formulation containing 10% notified chemical did not elicit a positive sensitisation response.

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 450 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 450 mg/kg bw/day (the highest dose tested) in the study, based on all treatment-related changes were either of no toxicological relevance or non-adverse due to their reversibility after the recovery period.

Mutagenicity/Genotoxicity
The notified chemical was negative in a bacterial reverse mutation assay but gave a positive response in an *in vitro* chromosome aberration test in Chinese hamster V79 cells. However the notified chemical tested negative in an *in vivo* mouse bone marrow micronucleus test via the oral route. The test substance was detected in plasma samples taken 1 h and 4 h after treatment, confirming the systemic distribution, and thus the bioavailability of the notified chemical.

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

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:

R38: Irritating to skin

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 effect of the notified chemical is as a skin irritant.

Reformulation
During reformulation, workers may be exposed to the notified chemical at up to 6.7% concentration. At this low proposed use concentration significant skin irritation effects are not expected. Furthermore, 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 0.5%. 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 ≤ 0.5% 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.

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 0.2848 mg/kg bw/day (see Section 6.1.2). Using a NOAEL of 450 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 1580. 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 ≤ 0.5% in fine fragrances, ≤ 0.1% in other cosmetics and ≤ 0.07% 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 formulations 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. In the event of spills, the product containing the notified chemical is expected to be collected with adsorbents, 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. Therefore, significant release of the notified chemical from this process to the environment is not expected. The process will be followed by automated filling of the formulated products into containers of various sizes suitable for retail and use. Wastes containing the notified chemical generated during reformulation include equipment wash water, residues in empty import containers and spilt materials. It is estimated by the notifier that up to 2% of the import volume of the notified chemical (or up to 20 kg) may be released from reformulation processes. These will be collected and released to sewers in a worst case scenario, or disposed of to landfill in accordance with local government regulations. Empty import containers are expected to be recycled or disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The notified chemical is expected to be released to the aquatic compartment through sewers during its use in various cosmetic 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 (or up to 10 kg), may remain in containers once the consumer products are used up. Wastes and residues 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

Following its use in cosmetic formulations and household products in Australia, the majority of the notified chemical is expected to enter the sewer system, before potential release to surface waters nationwide. Based on the results of ready biodegradability and inherent biodegradability studies, the notified chemical is not considered readily biodegradable (0% in 28 days). For details of the environmental fate studies, please refer to Appendix C. Based on its moderate water solubility and calculated low adsorption coefficient (log K_{OC} = 2.725),

release to surface waters may occur as limited partitioning to sludge and sediment is expected under environmental pH. Although the notified chemical is not readily biodegradable, it is not expected to be bioaccumulative due to its low partition coefficient (Log K_{OW} = 2.9). Therefore, in surface waters the notified chemical is expected to disperse and degrade through biotic and abiotic processes to form water and oxides of carbon.

The notified chemical is moderately volatile from water (vapour pressure = 1.2×10^{-3} kPa at 20 °C) and may slowly volatilise to air during sewage treatment. The half-life of the notified chemical in air is calculated to be 1.81 days, based on reactions with hydroxyl radicals (AOPWIN v1.92; US EPA, 2011). Therefore, the notified chemical is not expected to persist in the air compartment.

The majority of the notified chemical will be released to sewer after use. A small proportion of the notified chemical may be applied to land when effluent is used for irrigation, or when sewage sludge is used for soil remediation. The notified chemical may also be applied to land when disposed of to landfill as collected spills and empty container residue. The notified chemical in landfill, soil and sludge are expected to eventually degrade through biotic and abiotic processes to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

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

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	0%	
Daily effluent production:	4,523	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.606	µg/L
PEC - Ocean:	0.061	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1,000 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 1,500 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 the notified chemical in the applied soil in 5 and 10 years may be approximately 20.19 µg/kg and 40.39 µg/kg, respectively.

7.2. Environmental Effects Assessment

The results from an ecotoxicological investigation conducted on the notified chemical are summarised in the table below. Details of this study can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Daphnia Toxicity	48 h EC50 = 27 mg/L	Harmful to aquatic life

Based on the above ecotoxicological endpoint for the notified chemical, it is expected to be harmful 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 3; Harmful to aquatic life'. Based on the acute toxicity and lack of ready biodegradability of the notified chemical, it is formally classified as 'Chronic Category 3; Harmful to aquatic life with long lasting effects' under the GHS.

7.2.1. Predicted No-Effect Concentration

The predicted no-effects concentration (PNEC) has been calculated from the available endpoint for daphnia. A safety factor of 1,000 was used given a single acute endpoint for aquatic invertebrates is available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (*Daphnia*, 48 h)	27	mg/L
Assessment Factor	1,000	
Mitigation Factor	1.00	
PNEC:	27	µg/L

7.3. Environmental Risk Assessment

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

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q – River	0.606	27	**0.022**
Q – Ocean	0.061	27	**0.002**

The risk quotient for discharge of treated effluents containing the notified chemical to the aquatic environment indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in surface waters, based on its maximum annual importation quantity. Although the notified chemical is not readily biodegradable, it is expected to have a low potential for bioaccumulation. 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

Freezing Point < -50 °C

Method	OECD TG 102 Melting Point/Melting Range.
Remarks	Determined using a crystallising apparatus.
Test Facility	Givaudan (2004a)

Boiling Point 251 °C at 101.3 kPa (extrapolated)

Method	OECD TG 103 Boiling Point. OECD TG 104 Vapour Pressure.
Remarks	Dynamic method. The normal boiling point was extrapolated from the temperature/pressure relationship.
Test Facility	Givaudan (2004b)

Density 1,022 kg/m^3 at 20 °C

Method	OECD TG 109 Density of Liquids and Solids.
Remarks	Oscillating densitimeter method
Test Facility	Givaudan (2005)

Vapour Pressure 1.2×10^{-3} kPa at 20 °C

Method	OECD TG 104 Vapour Pressure.
Remarks	Static method
Test Facility	Notox (2004a)

Water Solubility 0.446 g/L at 20 °C

Method	OECD TG 105 Water Solubility.
Remarks	Flask Method
Test Facility	Givaudan (2004c)

Partition Coefficient (n-octanol/water) log Pow = 2.9

Method	OECD TG 117 Partition Coefficient (n-octanol/water).
Remarks	Reverse Phase HPLC Method
Test Facility	Givaudan (2004d)

Flash Point 120 °C at 101.3 kPa

Method	EC Council Regulation No 440/2008 A.9 Flash Point.
Remarks	Closed cup method
Test Facility	Givandan (2004e)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain	Rat/HanBrl:WIST
Vehicle	Polyethylene glycol 300
Remarks - Method	No significant protocol deviations

RESULTS

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

LD50	> 2000 mg/kg bw
Signs of Toxicity	One animal was killed in extremis due to ethical reasons on Day 2. Clinical signs noted in the surviving animals included ruffled fur, ataxia, hunched posture, sedation, ventral recumbency and bradypnea.
Effects in Organs	No macroscopic findings were noted at necropsy.
Remarks - Results	The body weight of the animals was within the range commonly recorded for this strain and age.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	RCC (2004a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test.
Species/Strain	Rat/HanRCC:WIST
Vehicle	None
Type of dressing	Semi-occlusive
Remarks - Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	2000	0/10

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	Slight general erythema was noted in 2 male animals on Day 2 and persisted in one of them up to Day 5. Slight formation of crusts was noted in 2 male animals from Day 6 to Day 7, or Day 9, respectively.
Signs of Toxicity - Systemic	No signs of systemic toxicity were noted.
Effects in Organs	No abnormalities were noted at necropsy.
Remarks - Results	The body weight of the animals was within the range commonly recorded for this strain and age.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	RCC (2005)

B.3. Irritation – skin

TEST SUBSTANCE Notified chemical

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3
Vehicle None
Observation Period 10 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	2.0	2.0	1.0	2	< 7 days	0
Oedema	0.3	0.3	0.3	1	< 48 h	0

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

Remarks - Results No mortality or signs of systemic toxicity were noted.

Very slight erythema was noted in all animals at 1-hour observation. Very slight to well-defined erythema was noted in all animals up to 72-hour observation. Very slight oedema was noted in all animals at 1- and 24-hour observations. Scaling was visible in two animals 7 days after treatment.

All signs of irritation were resolved at the end of the observation period (10 days).

CONCLUSION The notified chemical is irritating to the skin.

TEST FACILITY RCC (2004b)

B.4. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3 (1M, 2F)
Observation Period 72 hours
Remarks - Method No significant protocol deviations

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0	0.3	0.3	2	< 48 h	0
Conjunctiva: chemosis	0	0	0	1	< 24 h	0
Conjunctiva: *discharge*	0	0	0	1	< 24 h	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	-	0

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

Remarks - Results Slight to moderate reddening of the conjunctivae was noted in all animals at the 1-hour observation which persisted in two animals at the 24-hour

observation. Slight chemosis of the conjunctivae was observed in two animals at the 1 hour observation. Slight to moderate ocular discharge was noted in all animals at the 1-hour observation.

All signs of irritation were resolved at the 48-hour observation.

There were no mortality or clinical signs of systemic toxicity.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY RCC (2004c)

B.5. 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/Ca
Vehicle Acetone/olive oil (4:1)
Preliminary study No
Positive control Not conducted in parallel with the test substance, but had been conducted previously in the test laboratory.
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)	4F	693.9	-
1%	4F	870.8	1.25
10%	4F	724.1	1.04
30%	4F	1370.1	1.97
100%	4F	2053.3	2.96

EC3 Could not be calculated as the test substance at 100% concentration induced an SI of 2.96 (< 3).
Remarks - Results No local effects or systemic toxicity were noted. One animal in the 100% concentration group died on Day 2 post-application which was not considered by the study authors to be treatment-related as there were no clinical signs of toxicity.

CONCLUSION There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY RCC (2004d)

B.6. Skin sensitisation – human volunteers

TEST SUBSTANCE Formulation containing 10% notified chemical

METHOD Repeated insult patch test (RIPT)
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 hours (or 48 hours for patches applied on Friday).
Rest Period: ~14 days
Challenge Procedure: A patch was applied to an untreated site. Patches

	were removed by the applicants after 24 hours. Sites were graded 24 and 72 hours (if exhibiting reactions) post-application.
Study Group	90F, 20M; age range 18-74 years
Vehicle	None
Remarks - Method	Occluded. Patch was a modified Parke-Davis Readi-Bandage.

RESULTS

Remarks - Results	97/110 subjects completed the study. No withdrawals were related to the application of the test substance. No skin reactions were noted throughout the study.
CONCLUSION	The notified chemical was non-sensitising under the conditions of the test.
TEST FACILITY	Essex (2006)

B.7. Repeat dose toxicity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
Species/Strain	Rat/Wistar
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	Polyethylene glycol 300
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	450	0/10
control recovery	5 per sex	0	0/10
high dose recovery	5 per sex	450	0/10

Mortality and Time to Death

There were no unscheduled deaths.

Clinical Observations

Dyspnea was noted in male and female animals at 150 and 450 mg/kg/day and breathing noises were noted in males treated with 450 mg/kg/day. These findings disappeared during the recovery period and were therefore not considered by the study authors to be adverse. Ruffled fur was noted in 4/10 male animals treated with 450 mg/kg/day.

No changes in grip strength and locomotor activity were noted.

Moderate treatment-related decrease in absolute food consumption was noted in male animals treated with 450 mg/kg/day and slight decrease in relative food consumption was noted in male animals treated with 150 and 450 mg/kg/day. These findings were not considered by the study authors to be adverse due to their reversibility after the recovery period. No test item-related changes in food consumption were noted in male animals treated with 50 mg/kg/day and in female animals at any dose level.

Slight to moderate treatment-related decrease in body weight was noted in male animals treated with 450 mg/kg/day and slight to moderate decrease in body weight gain was noted in male animals treated with 150 and 450 mg/kg/day. These findings disappeared during the recovery period and were therefore not considered by the

study authors to be adverse. No treatment-related changes in body weight and body weight gain were noted in male animals treated with 50 mg/kg/day and in female animals at any dose level.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Haematology
Treatment-related and dose-dependent decrease in red blood cell count (RBC), haemoglobin (HB) and haematocrit (HCT) was noted in female animals treated with 50, 150 and 450 mg/kg/day. The relative and absolute reticulocyte count was consequently increased in female animals treated with 50, 150 and 450 mg/kg/day. These findings were not considered by the study authors to be adverse due to their reversibility after the recovery period.

Clinical biochemistry
Treatment-related increase in triglycerides (Trigly) level and gamma-glutamyl transferase (GGT) was noted in animals treated with 450 mg/kg/day at the end of the treatment. Animals treated with 450 mg/kg/day and female animals treated with 150 mg/kg/day showed an increased total blood protein level which was related to an increase of the respective globulin level at the end of the treatment. The albumin/globulin ratio (A/G ratio) was consequently decreased in female animals treated with 150 and 450 mg/kg/day. All these findings were considered by the study authors to be of adaptive nature and to be non-adverse due to their reversibility after the recovery period.

Urinalysis
No treatment-related changes in urinalysis were noted after 4 and 6 weeks.

Effects in Organs

Organ weights
Treatment-related increase in absolute and relative liver organ weight in animals treated with 50, 150 and 450 mg/kg/day was noted at the end of the treatment period. These differences were considered by the study authors to be an adaptive response and therefore of no toxicological relevance.

Treatment-related increase in absolute and relative adrenal organ weight in male animals treated with 50, 150 and 450 mg/kg/day and in female animals treated with 150 and 450 mg/kg/day was noted at the end of the treatment period, which was more clearly expressed in males than in females. These findings were considered by the study authors to be of stress-related nature and therefore of no toxicological relevance.

Treatment-related increase in absolute and relative spleen organ weight in female animals treated with 150 and 450 mg/kg/day was noted at the end of the treatment period. These findings were considered by the study authors to be a secondary effect, the extramedullary haematopoesis of the spleen, due to the anemia, and therefore of no toxicological relevance.

Treatment-related decrease in absolute and relative ovary organ weight in female animals treated with 450 mg/kg/day was noted at the end of the treatment period. These findings were considered by the study authors to be of no toxicological relevance due to lack of microscopical correlations.

All changes in organ weights were reversible after the recovery period.

Macroscopic findings
No treatment-related macroscopic findings were observed at the end of the treatment and recovery periods.

Microscopic findings
Treatment-related microscopic findings were noted in the liver, adrenal and vagina of animals treated with 150 and 450 mg/kg/day. The study authors stated that the microscopic changes in the liver were of adaptive character, and the findings in the adrenals were likely due to stress, therefore both findings were considered of no toxicological relevance. The reason for the changes in the vagina remained unclear. All these changes disappeared after the recovery period and were therefore considered not to be adverse.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 450 mg/kg bw/day in this study, based on all treatment-related changes were either of no toxicological relevance or non-adverse due to their reversibility after the recovery period.

TEST FACILITY RCC (2007)

B.8. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
Plate incorporation procedure (Test 1)/Pre incubation procedure (Test 2)
Species/Strain *S. typhimurium*: TA1535, TA1537, TA98, TA100, TA102
Metabolic Activation System S9 mix from β-naphthoflavone/sodium phenobarbitone induced rat liver
Concentration Range in Main Test Test 1
a) With metabolic activation: 3-5000 µg/plate
b) Without metabolic activation: 3-5000 µg/plate
Test 2
a) With metabolic activation: 1-5000 µg/plate
b) Without metabolic activation: 1-5000 µg/plate
Vehicle Ethanol
Remarks - Method A dose range-finding study was carried out at 3-5000 µg/mL. The dose selection for the main tests (the dose-range study was reported as Test 1) was based on toxicity observed in the range-finding study.

Positive controls:
With metabolic activation: 2-aminoanthracene
Without metabolic activation: sodium azide (TA1535, TA100); methyl methanesulfonate (TA102); 4-nitro-o-phenylene-diamine (TA1537, TA98)

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 333	> 5000	negative
Test 2	> 100	> 5000	negative
Present			
Test 1	> 333	> 5000	negative
Test 2	> 333	> 5000	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 RCC (2004e)

B.9. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical

METHOD OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Species/Strain Chinese hamster

Cell Type/Cell Line	V79
Metabolic Activation System	S9 mix from β-naphthoflavone/sodium phenobarbitone induced rat liver
Vehicle	Ethanol
Remarks - Method	A dose range-finding study was carried out at 13.7 – 1750 µg/mL. The dose selection for the main experiments was based on toxicity observed in the range-finding study. Vehicle and positive controls (ethyl methanesulfonate and cyclophosphamide) were run concurrently with the notified chemical.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	7.8, 15.6 31.3*, 62.5*, 125*, 250	4 h	18 h
Present			
Test 1	3.9, 7.8*, 15.6*, 31.3*, 62.5, 125	4 h	18 h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 109.4	> 125	> 218.8[#]	negative
Test 2 (24 hours exposure)[#]			> 218.8[#]	
Present				
Test 1	> 27.3	> 31.3	> 218.8[#]	positive

[#] In the Preliminary Test

Remarks - Results	In the absence of metabolic activation, a dose-dependent increase of aberrant metaphase cells was noted at the concentration of 31.3, 62.5 and 125 µg/mL. This funding was considered by the study authors to be biologically irrelevant as the cell values were within the testing facility's historical control data range. In the presence of metabolic activation, a dose-dependent increase in cells carrying structural chromosome aberrations was noted at 7.8, 15.6 and 31.3 µg/mL. The increase at 31.3 µg/mL was statistically significant and clearly exceeded the testing facility's historical control data range. The number of cells carrying exchanges was also distinctly increased at 31.3 µg/mL. The results of the positive controls confirmed the validity of the test system.
CONCLUSION	The notified chemical was clastogenic to Chinese hamster V79 cells treated *in vitro* under the conditions of the test.
TEST FACILITY	RCC (2006a)

B.10. Genotoxicity – in vivo

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
Species/Strain	Mouse/NMRI
Route of Administration	Oral – gavage
Vehicle	Corn oil
Remarks - Method	Six preliminary toxicity studies were carried out in each 2 male and 2

female animals were dosed once at 100, 500, 1000, 1250, 1500 and 2000 mg/kg bw respectively and observed for 48 hours. Following treatment one animal died and all animals showed reduced activity. The dose selection for the main experiment was based on the clinical signs of toxicity observed in the preliminary studies.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
vehicle control	5 per sex	0	24 h
low dose	5 per sex	312.5	24 h
mid dose	5 per sex	625	24 h
high dose 1	5 per sex	1250	24 h
high dose 2	5 per sex	1250	48 h
positive control, CP	5 per sex	40	24 h

CP=cyclophosphamide

RESULTS

Doses Producing Toxicity	One female animal in the high dose 2 group died after treatment and was substituted with a reserve animal. No clinical signs of toxicity was noted in the low dose group and reduction of spontaneous activity and ruffled fur were noted in the mid dose group. Clinical signs of toxicity noted in the high dose groups included reduction of spontaneous activity, abdominal position, eyelid closure, ruffled fur, stagger and difficulty in breathing. The test substance did not show any cytotoxic effects in the bone marrow (measured by the number of polychromatic erythrocytes (PCEs) per 2000 erythrocytes) but the bioanalytical data confirmed the systemic distribution of the test substance. The plasma samples taken 1 h and 4 h after treatment contained quantifiable amounts of the test substance.
Genotoxic Effects	There were no biologically relevant or statistically significant increases in the frequency of micronucleated PCEs.
Remarks - Results	The positive and negative controls gave a satisfactory response confirming the validity of the test system.

CONCLUSION The notified chemical was not genotoxic under the conditions of this *in vivo* mammalian erythrocyte micronucleus test.

TEST FACILITY RCC (2006b)

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 sewage sludge
Exposure Period	29 days
Auxiliary Solvent	None
Analytical Monitoring	Theoretical Oxygen Demand (ThOD)
Remarks - Method	The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
7	0	7	78
14	0	14	80
21	0	21	81
29	0	29	81

Remarks - Results	All validity criteria for the test were satisfied. The percentage degradation of the reference compound surpassed the threshold level of 60% by 5 days (73%). Therefore, the tests indicate the suitability of the inoculum. The degree of degradation of the test substance after 28 days was 0%. Therefore, the test substance is not considered to be readily biodegradable according to the OECD (301 F) guideline.
CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	Givaudan (2004f)

C.1.2. Inherent biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 302 C Inherent Biodegradability: Modified MITI Test (II).
Inoculum	Activated sewage sludge
Exposure Period	29 days
Auxiliary Solvent	None
Analytical Monitoring	Theoretical Oxygen Demand (ThOD)
Remarks – Method	The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
7	0	7	78
14	0	14	80
21	0	21	81
29	0	29	81

Remarks – Results	All validity criteria for the test were satisfied. The percentage degradation of the reference compound surpassed the threshold level of 60% by 5 days (73%). Therefore, the tests indicate the suitability of the inoculum. The

degree of degradation of the test substance after 28 days was 0%. Therefore, the test substance is not considered to be inherently biodegradable according to the OECD (302 C) guideline.

CONCLUSION The notified chemical is not inherently biodegradable.

TEST FACILITY Givaudan (2004g)

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.

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Concentration mg/L		*Number of D. magna*	*Cumulative Immobilised (%)*	
Nominal	*Actual*		*24 h*	*48 h*
Control	Control	20	5	10
10	8.58	20	0	0
18	15.7	20	10	10
32	28.9	20	15	60
56	51.3	20	80	100
100	92.8	20	100	100

EC50	27 mg/L (95% CI 24-32 mg/L) at 48 hours
NOEC	10 mg/L at 48 hours
Remarks - Results	All validity criteria for the test were satisfied. The test solutions were not renewed during the 48 h test period. The actual concentrations of the test substance were measured at the start and end of the 48 h test period. As measured concentrations were within 20% difference of the nominal concentrations, the nominal concentrations were used. The 48 h EC50 and NOEC for daphnids were determined to be 27 mg/L (95% CI 24-32 mg/L) and 10 mg/L, respectively, based on nominal concentrations.

CONCLUSION The notified chemical is considered to be harmful to aquatic invertebrates.

TEST FACILITY Notox (2004b)

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.

Essex (2006) Clinic Safety Evaluation Repeated Insult Patch Test (Panel No. 06055, Entry No. 12409.05, December, 2006). Verona, NJ, USA, Essex Testing Clinic Inc (Unpublished report submitted by the notifier).

Givaudan (2004a) Determination of the Freezing Point of GR-85-4441 according to OECD Guideline No. 102 (Method of the Freezing Temperature) (Study No. 04-E044, October, 2004). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2004b) Vapour Pressure Curve of GR-85-4441 according to OECD Guideline No. 104 and Determination of the Boiling Point (Study No. 04-E046, October, 2004). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2004c) Water Solubility of GR-85-4441 According to OECD Guideline No. 105 (Flask Method) (Study No. 04-E063; 23 November 2004). Vernier/Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2004d) Partition Coefficient n-octanol/Water of GR-85-4441 According to OECD Guideline No. 117 (Study No. 04-E056; 14 October 2004). Vernier/Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2004e) Flash Point of GR-85-4441 according to DIN 51758 (Study No. 04-E048, October, 2004). Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2004f) Ready Biodegradability of GR-85-4441 According to OECD Guideline No. 301F (Study No. 04-E050, November, 2004). Vernier/Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2004g) Inherent Biodegradability of GR-85-4441 According to OECD Guideline No. 302C (Study No. 04-E052, December, 2004). Vernier/Geneva, Switzerland, Givaudan Suisse SA (Unpublished report submitted by the notifier).

Givaudan (2005) Determination of the Density of GR-85-4441 according to OECD Guideline No. 109 (Oscillating Densitimeter) (Study No. 04-E042 (A1), February, 2005). 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.

Notox (2004a) Determination of the Vapour Pressure of GR-85-4441 by the Static Method (Project No. 413775, September, 2004). S'-Hertogenbosch, The Netherlands, Notox B.V. (Unpublished report submitted by the notifier).

Notox (2004b) Acute Toxicity Study in *Daphnia magna* with GR-85-4441 (Static) (Study No. 413786, September, 2004). S'-Hertogenbosch, The Netherlands, Notox B.V. (Unpublished report submitted by the notifier).

RCC (2004a) GR-85-4441: Acute Oral Toxicity Study in Rats (Study No. 854803, September, 2004). Fullinsdorf, Switzerland, RCC Ltd (Unpublished report submitted by notifier).

RCC (2004b) GR-85-4441: Primary Skin Irritation Study in Rabbits (4-our Semi-Occlusive Application) (Study No. 854804, September, 2004). Fullinsdorf, Switzerland, RCC Ltd (Unpublished report submitted by notifier).

RCC (2004c) GR-85-4441: Primary Eye Irritation Study in Rabbits (Study No. 854805, October, 2004). Fullinsdorf, Switzerland, RCC Ltd (Unpublished report submitted by notifier).

RCC (2004d) Local Lymth Node Assay (LLNA) in Mice with GR-85-4441 (Study No. 842303, August, 2004). Itingen, Switzerland, RCC Ltd (Unpublished report submitted by notifier).

RCC (2004e) *Salmonella Typhimurium* Reverse Mutation Assay with GR-85-4441 (Study No. 837300, September, 2004). Rossdorf, Germany, RCC Cytotest Cell Research GmbH (Unpublished report submitted by notifier).

RCC (2005) Safraleine: Acute Dermal Toxicity Study in Rats (Study No. A25795, September, 2005). Fullinsdorf, Switzerland, RCC Ltd (Unpublished report submitted by notifier).

RCC (2006a) *In Vitro* Chromosome Aberration Test in Chinese Hamster V79 Cells with Safraleine (Study No. 905407, February, 2006). Rossdorf, Germany, RCC Cytotest Cell Research GmbH (Unpublished report submitted by notifier).

RCC (2006b) Micronucleus Assay in Bone Marrow Cells of the Mouse with Safraleine (Study No. 1002802, September, 2006). Rossdorf, Germany, RCC Cytotest Cell Research GmbH (Unpublished report submitted by notifier).

RCC (2007) Safraleine: 28-Day Oral Toxicity (Gavage) Study in the Wistar Rat (Study No. B10440, August, 2007). Itingen, Switzerland, RCC Ltd (Unpublished report submitted by notifier).

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.

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

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 >.

US EPA (2011) Estimation Programs Interface (EPI) Suite™ for Microsoft® Windows, v 4.10. United States Environmental Protection Agency. Washington DC, USA.