File No: LTD/1949

January 2017

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Benzene, 1-(cyclopropylmethyl)-4-methoxy-

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

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

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Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/1949	Givaudan Singapore Pte Ltd	Benzene, 1-(cyclopropylmethyl)-4-methoxy-	Yes	< 1 tonne per annum	Fragrance ingredient for household and cosmetic products

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 Sensitiser (Category 1B)	H317 – May cause an allergic skin reaction

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 ≤ 0.36% concentration in cosmetic and household products, the notified chemical is not considered to pose an unreasonable risk to public health.

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

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Category 1B Skin Sensitiser: 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.

- Due to the skin sensitisation properties of the notified chemical, the notifier should consider their obligations under the Australian Dangerous Goods Code.

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 allergic skin reaction.

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical during reformulation:
  - Adequate local ventilation
  - Enclosed/automated system

- 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 formation of vapour, mist or aerosol
  - Avoid contact with skin and eyes

- 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
  - Goggles
  - Impervious gloves

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System 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.

Storage

- The handling and storage of the notified chemical should be in accordance with the Safe Work Australia Code of Practice for *Managing Risks of Hazardous Chemicals in the Workplace* (SWA, 2012) or relevant State or Territory Code of Practice.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by an inert, inorganic, non-combustible absorbent material 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 use concentration of the notified chemical exceeds or is likely to exceed 0.36% in cosmetic and household products;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a fragrance ingredient for household and cosmetic products, 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
Givaudan Singapore Pte Ltd (ABN: 79 368 011 578)
1 Pioneer Turn
SINGAPORE SG 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 (2003)
USA (2003)
Canada (2005)
China (2006)
Philippines (2006)

2. IDENTITY OF CHEMICAL

MARKETING NAME
Toscanol

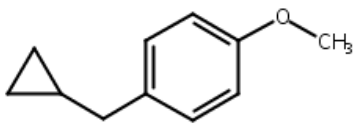
CAS NUMBER
16510-27-3

CHEMICAL NAME
Benzene, 1-(cyclopropylmethyl)-4-methoxy-

OTHER NAME
Cyclopropyl Estragole

MOLECULAR FORMULA
$C_{11}H_{14}O$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
162.23 Da

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

3. COMPOSITION

DEGREE OF PURITY
> 98%

HAZARDOUS IMPURITIES
None identified

NON HAZARDOUS IMPURITIES (> 1% BY WEIGHT)
None identified

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: colourless liquid

Property	Value	Data Source/Justification
Freezing Point	-23 °C	Measured
Boiling Point	235 °C at 101.3 kPa	Measured
Density	990 kg/m^3 at 20 °C	Measured
Vapour Pressure	1.13 × 10^{-3} kPa at 20 °C	Measured
Water Solubility	46.7 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	No hydrolysable functionality
Partition Coefficient (n-octanol/water)	Log Pow = 3.8 at 35 °C	Measured
Surface Tension	65.6 mN/m at 20 °C	Measured
Adsorption/Desorption	Log K_{oc} = 3.1	Calculated using KOCWIN v2.00 (US EPA, 2011)
Dissociation Constant	Not determined	Not expected as the chemical does not contain dissociable functionalities
Flash Point	113 °C at 101.3 kPa	Measured
Flammability	Combustible liquid*	Based on measured flash point
Autoignition Temperature	> 400 °C	Measured
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidative properties

* Based on *Australian Standard AS1940* definitions

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.

The notified chemical has a flash point of 113 °C. Based on *Australian Standard AS1940* definitions for combustible liquids, a liquid that has a flash point of 150 °C or less is a Class C1 combustible liquid.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. It will be imported in fragrance formulations at ≤ 4.6% concentration for further reformulation into cosmetic and household products.

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

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

PORT OF ENTRY
Sydney and Perth

TRANSPORTATION AND PACKAGING
The notified chemical will be imported as a component of fragrance formulations in 1, 5, 10, 25, 100 or 190 kg glass or lacquer-lined containers and transported to reformulation sites within Australia by road. The finished end-use consumer products will be packaged in containers suitable for retail sale.

USE
The notified chemical will be used as a fragrance ingredient. The proposed use concentrations in finished consumer products are shown below:

Product Type	*Maximum Use Concentration (%)*
Fine fragrances	0.36
Cosmetics	0.0675
Household cleaning products	0.046
Fabric care products	0.0175

OPERATION DESCRIPTION
The notified chemical will not be manufactured within Australia. No repackaging of imported fragrance formulations containing the notified chemical will occur. The imported fragrance formulations containing the notified chemical at ≤ 4.6% concentration will be stored at the notifier's facilities until distribution to customer facilities for reformulation into end-use consumer products.

Reformulation
The procedures for incorporating the notified chemical into end-use consumer products will likely vary depending on the nature of the formulated products and may involve both automated and manual transfer steps. In general, it is expected that, during reformulation processes, the notified chemical will be measured and added to the mixing tank where it will be blended with additional components to form the finished cosmetic and household products. Blending processes will be followed by automated filling of the formulated products into consumer containers in various sizes. The operations are expected to be highly automated and use closed systems with adequate ventilation. During the reformation processes, samples containing the notified chemical at various stages will be taken for quality control testing.

End use
Cosmetic products
The finished cosmetic products containing the notified chemical will be used by consumers and professionals such as beauticians and hairdressers. Depending on the nature of the products, applications may be by hand, spray or through the use of applicators.

Household products
Household products containing the notified chemical may be used by consumers and professional workers such as cleaners. The products may be used in either closed systems with episodes of controlled procedures, for instance automatic washing machine cycles, or open manual processes including spraying, brushing, dipping, wiping and rinsing.

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	Incidental	Incidental
Mixer (plant operators)	4	2
Drum handling	4	2
Maintenance	4	2
Quality control	4	2
Packagers	4	2
End users (professionals)	1-8	200

EXPOSURE DETAILS

Transport and storage

Transport and storage workers may come into contact with the notified chemical as a component of fragrance formulations or consumer products, only in the unlikely event of accidental rupture of the drum containers.

Reformulation

During reformulation at consumer sites, dermal, ocular and possible inhalation exposure of workers to the notified chemical at ≤ 4.6% concentration may occur during measuring, transfer, blending, sampling, and cleaning/maintenance of equipment. The exposure is expected to be minimised by the use of engineering controls including adequate local ventilation and enclosed systems, and by the use of PPE such as coveralls, goggles, impervious gloves as stated by the notifier in the submission.

End-use

Exposure to the notified chemical in end-use products (at ≤ 0.36% concentration) may occur in professions where the services provided involve the application of cosmetic products to clients (i.e., hair and beauty salons), or the use of cleaning 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 appropriate PPE is used, exposure of such workers to the notified chemical is expected to be of a similar or lesser extent than that experienced by consumers using the same products.

6.1.2. Public Exposure

There will be widespread and repeated exposure of the public to the notified chemical at ≤ 0.36% concentration through the use of a wide range of cosmetic and household products. The principal routes of exposure will be dermal, while ocular and inhalation exposure (e.g., through the use of spray products) is also possible.

Data on typical use patterns of various types of consumer products 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 exposure assessment via the dermal route, Australian use patterns for various products are assumed to be similar to the consumer use patterns in Europe. In the absence of dermal absorption data and based on the low molecular weight of the notified chemical (162.23 Da), a dermal absorption (DA) of 100% was assumed (European Commission, 2003). For inhalation exposure estimation of spray products, a 2-zone approach was used (Steiling *et al*., 2014; Rothe *et al*., 2011; Earnest, Jr, 2009) with an adult inhalation rate of 20 m^3/day (enHealth, 2012). It was conservatively assumed that the fraction of the notified chemical inhaled would be 50%, with the remainder ending up on the targets as intended. A lifetime average female body weight (BW) of 64 kg (enHealth, 2012) was applied in the calculations.

Cosmetic products (dermal exposure)

Product type	*Amount (mg/day)*	*Chemical concentration (%)*	*Retention Factor (RF)*	*Daily systemic exposure (mg/kg bw/day)*
Body lotion	7,820	0.0675	1.00	0.0825
Face cream	1,540	0.0675	1.00	0.0162
Hand cream	2,160	0.0675	1.00	0.0228

Product type	*Amount (mg/day)*	*Chemical concentration (%)*	*Retention Factor (RF)*	*Daily systemic exposure (mg/kg bw/day)*
Fine fragrance	750	0.36	1.00	0.0422
Deodorant	1,430	0.0675	1.00	0.0151
Shampoo	10,460	0.0675	0.01	0.0011
Conditioner	3,920	0.0675	0.01	0.0004
Shower gel	18,670	0.0675	0.01	0.0020
Hand wash soap	20,000	0.0675	0.01	0.0021
Hair styling products	4,000	0.0675	0.10	0.0042
Total				**0.1886**

Daily systemic exposure = (Amount × Chemical concentration × RF × DA)/BW (RF = retention factor; DA = dermal absorption; BW = body weight)

Household Products (Indirect dermal exposure – from wearing clothes)

Product type	*Amount (g/use)*	*C (%)*	*Product Retained (%)*	*Product Transferred (%)*	*Daily systemic exposure (mg/kg bw/day)*
Laundry liquid	230	0.046	0.95	10	0.0016
Fabric softener	90	0.0175	0.95	10	0.0002
Total					**0.0018**

Daily systemic exposure = (Amount × C × PR × PT × DA)/BW (C = chemical concentration; PR = product retained; PT = product transferred; DA = dermal absorption; BW = body weight)

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*	*Daily systemic exposure (mg/kg bw/day)*
Laundry liquid	1.43	0.046	1,980	0.01	0.01	0.007	0.0000
Dishwashing liquid	3	0.046	1,980	0.009	0.01	0.03	0.0001
All-purpose cleaner	1	0.046	1,980	1	0.01	0.007	0.0010
Total							**0.0011**

Daily systemic exposure = Frequency × C × Contact Area × Product Usage × Film Thickness × Time Scale Factor × DA/ BW (C = chemical concentration; DA = dermal absorption; BW = body weight)

Aerosol products (Inhalation exposure)

Product type	*Amount (g/day)*	*C (%)*	*Exposure Duration Zone 1 (min)*	*Exposure Duration Zone 2 (min)*	*Volume Zone 1 (m^3)*	*Volume Zone 2 (m^3)*	*Daily systemic exposure (mg/kg bw/day)*
Hairspray	9.89	0.0675	1	20	1	10	**0.0022**

Daily systemic exposure = [(Amount × C × 20 m^3/day Inhalation Rate × 50% Fraction Inhaled × 0.1) / BW × 1440)] × (Exposure Duration Zone 1/Volume Zone 1 + Exposure Duration Zone 2/Volume Zone 2) (C = chemical concentration; BW = body weight)

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above tables that contain the notified chemical. This would result in a combined internal dose of 0.1937 mg/kg bw/day for the chemical. 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 and deodorants).

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 > 2,000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2,000 mg/kg bw; low toxicity

Endpoint	*Result and Assessment Conclusion*
Rabbit, skin irritation	moderately irritating
Mouse, skin sensitisation – Local lymph node assay	evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* mammalian chromosome aberration test	non genotoxic

Toxicokinetics
No toxicokinetic data was provided for the notified chemical. Based on the water solubility (46.7 g/L at 20 ºC), partition coefficient (log Pow = 3.8 at 35 °C) and low molecular weight (162.23 Da) of the notified chemical, absorption across biological membranes is expected to occur.

Acute toxicity
The notified chemical was found to be of low acute oral and dermal toxicity in rats. No acute inhalation toxicity data were provided.

Irritation
The notified chemical was found to be moderately irritating to skin in a study conducted in rabbits. Irritation effects observed included erythema, oedema and scaling which, with the exception of scaling in one animal, were reversible within 14 days. However, the irritation scores did not warrant hazard classification under GHS as adopted for industrial chemicals in Australia.

No information is available on the eye irritation potential of the notified chemical.

Sensitisation
The notified chemical was tested for skin sensitisation potential in a mouse local lymph node assay (LLNA). The Stimulation Indices were 0.5, 1.1, 2.8, and 5.5 with the notified chemical at 0.1%, 1%, 10% and 100% (undiluted) concentration, respectively. An EC3 value of 16.7% was obtained. Based on the results of this study, the notified chemical is considered a skin sensitiser (Category 1B) under the GHS.

Repeated dose toxicity
No information is available on the repeated dose toxicity of the notified chemical.

Mutagenicity/Genotoxicity
The notified chemical was not considered to be mutagenic in a bacterial reverse mutation assay when tested in *Salmonella typhimurium* strains with and without metabolic activation. The notified chemical did not induce structural chromosome aberrations when tested in V79 cells of the Chinese hamster *in vitro* with and without metabolic activation. The notified chemical is unlikely to be of concern for mutagenic or genotoxic effects.

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 Sensitiser (Category 1B)	H317 – May cause an allergic skin reaction

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
The critical health effect of the notified chemical is as a skin sensitiser. Given the potential for the notified chemical to cross biological membranes, the potential for systemic toxicity cannot be ruled out. The notified chemical is also a mild skin irritant. The eye irritation potential of the notified chemical has not been determined.

Reformulation
Workers may experience dermal, ocular and perhaps inhalation exposure to the notified chemical at ≤ 4.6% concentration during reformulation. Given the notified chemical is a skin sensitiser caution should be exercised when handling the notified chemical during reformulation and quality control processes. The use of local ventilation, enclosed/automated processes and PPE (i.e., coveralls, goggles and impervious gloves) should minimise the potential for exposure.

Therefore, provided that adequate control measures are in place to minimise worker exposure, the risk to workers from use of the notified chemical is not considered to be unreasonable.

End use
Cleaners, hair and beauty care professionals may come into contact with the notified chemical at ≤ 0.36% concentration. Such professionals may use 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 (for details of the public health risk assessment, see Section 6.3.2).

6.3.2. Public Health

Irritation
The notified chemical is a mild skin irritant. The eye irritation potential of the notified chemical has not been determined. The main risk of irritation will be expected from use of cosmetic products containing the notified chemical. However, given the low proposed use concentration of the notified chemical in cosmetic products (i.e. ≤ 0.36%), significant skin and eye irritation effects are not expected.

Skin sensitisation
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 product that may contain the notified chemical (at 0.36% concentration), as a worst case scenario, the Consumer Exposure Level (CEL) for the notified chemical is estimated to be 13.50 μg/cm^2/day (Cadby *et al.,* 2002). When tested in an LLNA study, the notified chemical was a skin sensitiser with an EC3 value of 16.7%. Consideration of the study details and application of appropriate safety factors allowed the derivation of an Acceptable Exposure Level (AEL) of 13.75 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 (300 used for calculation).

As the CEL is estimated to be less than the AEL, the risk to the public of 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 the lower expected exposure level from other cosmetic 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.

Repeat dose toxicity
The repeated dose toxicity effects of the notified chemical have not been determined. However, exposure is expected to be limited by the low concentration of the notified chemical (≤ 0.36%) in end use products.

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at ≤ 0.36% concentration in cosmetic and household products is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The notified chemical will not be manufactured in Australia; therefore there will be no release of the notified chemical to the environment from this activity. 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. Accident leaks and spills of products containing the notified chemical are expected to be collected by inert absorbent materials and disposed of to landfill in accordance with local government regulations.

The reformulation process will involve in batch blending operations that is expected to 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, including 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 to landfill in accordance with local government regulations.

RELEASE OF CHEMICAL FROM USE
The notified chemical is expected to be released (> 98% of the total imported volume, as indicated by the notifier) 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 residues of the notified chemical in empty containers are likely to either share the fate of the containers 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 notified chemical is not readily biodegradable (no biodegradation in 28 days). However, the notified chemical is inherently biodegradable based on the results from an inherent biodegradability study (73% biodegradation in 57 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. Based on its calculated adsorption coefficient (log K_{oc} = 3.1), the notified chemical is expected to partially adsorb to sediment or any suspended particulate matter. A small proportion of the notified chemical may be applied to land 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 residues. The notified chemical in water, landfill, soil and sediment is expected to eventually degrade through biotic and abiotic processes to form water and oxides of carbon.

The notified chemical has potential to bioaccumulate in aquatic life based on its relatively high log Pow (log Pow = 3.8). However, significant bioaccumulation is not expected as the notified chemical is inherently biodegradable.

7.1.3. Predicted Environmental Concentration (PEC)
The calculation for the predicted environmental concentration (PEC) is summarised in the table below. Based on the reported use in cosmetics and household cleaning products, it is assumed that 100% of the total import volume of the notified chemical is released to the sewer treatment plants (STPs) and there is no removal of the notified chemical at STPs. The release is assumed to be nationwide over 365 days per year.

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	360	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 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 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 = 6.5 mg/L	Toxic to fish
Daphnia Toxicity	48 h EC50 = 4.0 mg/L	Toxic to aquatic invertebrates
Algae Toxicity	96 h E_rC50 = 2.3 mg/L	Toxic to algae

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 non-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 of NOEC = 0.47 mg/L for Alga. 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		
NOEC (Alga)	0.47	mg/L
Assessment Factor	100	
PNEC:	4.70	µg/L

7.3. Environmental Risk Assessment

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.61	4.7	**0.129**
Q - Ocean	0.06	4.7	**0.013**

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

Freezing Point -23 °C

Method	OECD TG 102 Melting Point/Melting Range (1995)
Remarks	Freezing temperature method
Test Facility	Givaudan (2002a)

Boiling Point 235 °C at 101.3 kPa

Method	OECD TG 104 Vapour Pressure (as function of temperature) (1995)
Remarks	The vapour pressure curve as a function of temperature was determined using dynamic method. By extrapolation, the boiling point at 101.3 kPa was calculated. The 95% confidence limits were 234 – 237 °C at 101.3 kPa.
Test Facility	Givaudan (2002b)

Density 990 kg/m^3 at 20 °C

Method	OECD TG 109 Density of Liquids and Solids (1995)
Remarks	Oscillating density meter method
Test Facility	Givaudan (2002c)

Vapour Pressure 1.13×10^{-3} kPa at 20 °C

Method	OECD TG 104 Vapour Pressure
Remarks	Static technique
Test Facility	NOTOX (2002a)

Water Solubility 46.7 g/L at 20 °C

Method	OECD TG 105 Water Solubility EC Council Regulation No 440/2008 A.6 Water Solubility (92/69/EEC)
Remarks	Flask Method
Test Facility	Givaudan (2002e)

Partition Coefficient (n-octanol/water) log Pow = 3.8 at 35 °C

Method	OECD TG 117 Partition Coefficient (n-octanol/water) EC Council Regulation No 440/2008 A.8 Partition Coefficient, (91/69/EEC)
Remarks	HPLC Method/Flask Method
Test Facility	Givaudan (2002f)

Surface Tension 65.6 mN/m at 20 °C

Method	OECD TG 115 Surface Tension of Aqueous Solutions (1995) EC Council Regulation No 440/2008 A.5 Surface Tension (2008)
Remarks	Concentration: 90% of saturation concentration
Test Facility	Harlan (2011a)

Flash Point 113 °C at 101.3 kPa

Method	EC Commission Directive No 92/69/EEC A.9 Flash Point
Remarks	Pensky-Martens method
Test Facility	Givaudan (2002d)

Autoignition Temperature > 400 °C

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

Remarks	Flask method was used. Grey fumes were emitted when heated above 250 °C. No ignition of the test substance was observed up to 400 °C.
Test Facility	Harlan (2011b)

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 (SPF)
Vehicle	Polyethylene glycol 300 (PEG 300)
Remarks - Method	No significant deviations of protocol were noted. The purity of the test substance was reported to be at 99.1%.

RESULTS

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

LD50	> 2,000 mg/kg bw
Signs of Toxicity	Slightly ruffled fur and hunched posture were noted in one female 1 to 2 hours after the treatment. No other clinical signs were observed.
Effects in Organs	No macroscopic findings were recorded 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 (2002a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 402 Acute Dermal Toxicity
Species/Strain	Rat/HanRcc:WIST (SPF)
Vehicle	None
Type of dressing	Semi-occlusive
Remarks - Method	No significant deviations of protocol were noted. The purity of the test substance was reported to be at 99.6%.

RESULTS

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

LD50	> 2,000 mg/kg bw
Signs of Toxicity - Local	Slight general erythema was noted in four females on day 2 or 3 and persisted in three animals until day 3 or 4. Slight scaling was present in three females from day 3 to day 4 or 7. Slight formation of crusts was observed in one female from day 3 to day 7. No local effects were observed in the male animals.
Signs of Toxicity - Systemic	No clinical signs were observed during the course of the study.
Effects in Organs	No macroscopic findings were observed 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 14 days
Type of Dressing Semi-occlusive.
Remarks - Method No significant deviations of protocol were noted. The purity of the test substance was reported to be 99.1%

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	2.00	2.00	2.00	2	< 10 d	0
Oedema	0.33	0.33	0.33	2	< 48 h	0

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

Remarks - Results The application of the notified chemical to the skin resulted in moderate signs of irritation including erythema, oedema and scaling. With the exception of the scaling in one animal, these effects were reversible in 14 days.

CONCLUSION The notified chemical is moderately irritating to the skin.

TEST FACILITY RCC (2002b)

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/CaOlaHsd)
Vehicle Ethanol:water (7:3 v/v)
Preliminary study No
Positive control α-Hexylcinnamaldehyde
Remarks - Method No significant deviations of protocol were noted. The purity of the test substance was reported to be 99.1%.

RESULTS

Concentration (% w/w)	*Number and sex of animals*	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance			
0 (ethanol: water)	4 F	395	1.0
0.1	4 F	185	0.5
1	4 F	455	1.1
10	4 F	1126	2.8
100	4 F	2159	5.5
Positive Control			
0 (acetone: olive oil)	4 F	529	1.0
5	4 F	1521	2.9
10	4 F	1372	2.6
25	4 F	3732	7.1

EC3	16.7%
Remarks - Results	EC3 for the positive control was calculated to be 11.3% indicative of expected positive results.
CONCLUSION	There was evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.
TEST FACILITY	RCC (2002c)

B.5. Genotoxicity – bacteria reverse mutation test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test Plate incorporation procedure (Test 1) and pre incubation procedure (Test 2)
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 and TA102
Metabolic Activation System	Phenobarbital/β-naphthoflavone induced rat liver S9 fraction
Concentration Range in Main Test	Test 1 a) With metabolic activation: 10 to 2,500 µg/plate b) Without metabolic activation: 10 to 2,500 µg/plate Test 2 a) With metabolic activation: 3 to 1,000 µg/plate b) Without metabolic activation: 3 to 1,000 µg/plate
Vehicle	DMSO
Remarks - Method	No significant deviations of protocol were noted. Concentration range in the main tests was selected based on toxic effects observed in the pre-experiment. Only *Salmonella typhimurium* strains were tested. The purity of the test substance was reported to be 99.1%.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity in Preliminary Test*	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 1,000	≥ 333	> 2,500	Negative
Test 2	-	≥ 100	> 1,000	Negative
Present				
Test 1	≥ 333	≥ 333	> 2,500	Negative
Test 2	-	≥ 1,000	> 1,000	Negative

Remarks - Results	No substantial increase in revertant colony numbers of the test strains was observed in the presence or absence of metabolic activation. No clear dose response was noted. Results of the positive controls confirmed the sensitivity of the test strains.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	RCC (2002d)

B.6. Genotoxicity – *in vitro* mammalian chromosome aberration test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 473 *In vitro* Mammalian Chromosome Aberration Test
Species	Chinese hamster
Cell Line	V79
Metabolic Activation System	Phenobarbital/β-naphthoflavone induced rat liver S9 fraction

Vehicle	Ethanol
Remarks - Method	No significant deviations of protocol were noted. The purity of the test substance was reported to be 99.6%. Ethanol was used as a solvent for the test substance in the study and the final concentration of ethanol in the culture medium was 0.5%.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	3.1, 6.3, 12.5*, 25*, 50* and 100	4 h	18 h
Test 2	3.1, 6.3, 12.5*, 25*, 50* and 100	18 h	18 h
Test 3	12.5, 25.0, 50* and 100	28 h	28 h
Present			
Test 1	31.3*, 62.5*, 125*, 250, 500 and 1,000	4 h	18 h
Test 2	7.8, 15.6*, 31.3*, 62.5*, 125 and 250	4 h	28 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	≥ 51.6	≥ 100	> 100	Negative
Test 2	-	≥ 100	> 100	Negative
Test 3	-	≥ 100	> 100	Negative
Present				
Test 1	≥ 206.3	≥ 125	≥ 500	Negative
Test 2	-	≥ 62.5	> 250	Negative

Remarks - Results	In the absence of metabolic activation with18 hour continuous exposure, dose-related increases (maximum 2.5%) in the number of aberrant metaphase cells were observed in the test concentration range of 12.5 to 50 µg/mL. However, these increases were within the historical control data range (0.0 - 4.0 %) and therefore were considered by the study authors as biologically irrelevant. Positive controls induced expected positive results indicative of the sensitivity of the test system.
CONCLUSION	The notified chemical was not clastogenic to Chinese hamster V79 cells treated *in vitro* under the conditions of the test.
TEST FACILITY	RCC (2006)

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	35 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 not determined to have significantly adverse effects on bacterial respiration.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
5	0	5	69
7	0	7	79
14	0	14	88
21	0	21	92
28	0	28	96
35	0	35	98

Remarks - Results	Validity criteria for the test are satisfied. The percentage degradation of the reference compound (sodium benzoate) surpassed the threshold level of 60% after 5 days (69%), and attained 96% degradation in 28 days. Therefore, the tests indicate the suitability of the inoculum. No degradation of the test substance was observed after 28 days. 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 (2003)

C.1.2. Inherent biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 302C Inherent Biodegradability: Modified MITI test
Inoculum	Activated sludge
Exposure Period	57 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*
7	0	5	73
14	28	7	81
21	44	14	88
28	55	21	93
42	68	28	97
57	73		

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

The percentage degradation of the reference compound (sodium benzoate) surpassed the threshold level of 70% after 5 days (73%), and attained 97% degradation in 28 days. Therefore, the tests indicate the suitability of the inoculum. In 57 days the notified chemical was degraded over 70% (73%).

CONCLUSION: The notified chemical is inherently biodegradable

TEST FACILITY: Givaudan (2010)

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: Carp (*Cyprinus carpio,* Teleostei, Cyprinidae) (Linnaeus, 1758)
Exposure Period: 96 hours
Auxiliary Solvent: None
Water Hardness: 250 mg $CaCO_3$/L
Analytical Monitoring: HPLC
Remarks – Method: The study was conducted according to the above guideline without deviation from the protocol. The test media were renewed every 24 hours.

RESULTS

Nominal Concentration (mg/L)	*Number of Fish*	*Mortality*				
		3 h	*24 h*	*48 h*	*72 h*	*96 h*
Blank-Control	7	0	0	0	0	0
0.81	7	0	0	0	0	0
1.5	7	0	0	0	0	0
2.6	7	0	0	0	0	0
4.6	7	0	0	0	0	0
9.2	7	0	7	7	7	7

LC50: 6.5 mg/L at 96 hours (95% confidence limit: 4.6 – 9.2 mg/L)
Remarks – Results: All the validity criteria were satisfied.

No fish showed any abnormal behaviour (including mortality) in the control group.

At the concentration 9.2 mg/L of the notified chemical, 100% mortality was observed within 24 h.

CONCLUSION: The notified chemical is toxic to fish.

TEST FACILITY NOTOX (2002b)

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 None
Water Hardness 250 mg $CaCO_3$/L
Analytical Monitoring HPLC
Remarks - Method The test was conducted according to the above test guideline without significant deviation from the protocol.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Blank-Control	-	20	0	0
1.0	0.87	20	0	0
1.8	1.5	20	0	1
3.2	2.4	20	0	1
5.6	4.5	20	9	12
10	8.3	20	17	20

LC50 4.0 mg/L at 48 hours (95% confidence limit: 3.5-4.7 mg/L)

Remarks - Results All validity criteria were satisfied.

Based on measured concentration the 48 h EC_{50} was determined to be 4.8 mg/L.

CONCLUSION The notified chemical is toxic to aquatic invertebrate.

TEST FACILITY NOTOX (2002c)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE Notified chemical

METHOD OECD TG 201 Alga, Growth Inhibition Test - static.
Species *Selenastrum capricornutum*
Exposure Period 96 hours
Concentration Range Nominal: 1.0, 1.8, 3.2, 5.6 and 10.0 mg/L
Actual: 0.095, 0.195, 0.318, 0.618 and 1.09 mg/L
Auxiliary Solvent None
Water Hardness 250 mg $CaCO_3$/L
Analytical Monitoring HPLC
Remarks - Method The test was conducted according to the above test guideline without significant deviation from the protocol.

RESULTS

Biomass		*Growth*	
EC50 (mg/L at 96 h)	*NOEC (mg/L)*	*EC50 (mg/L at 96 h)*	*NOEC (mg/L)*
Not reported	Not reported	2.3 (95% confident limit:1.9 – 2.6)	0.47

Remarks - Results All validity criteria were satisfied.

	A distinct concentration decrease was observed throughout the test. The deviation from nominal to actual test concentration is well above ± 20%. According to the OECD test guideline if the deviation from the nominal or measured initial concentration is not within the range of ± 20%, analysis of the results should be based on geometric mean concentration, which was not followed. Therefore, the result may not reflect the actual toxicity level of the notified chemical toward the growth of algae and should be treated with caution.
CONCLUSION	The notified chemical is toxic to algae.
TEST FACILITY	NOTOX (2002d)

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