File No: LTD/2065

February 2019

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Heptane, 2-methoxy-2-methyl-

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/2065	Takasago International (Singapore) Pte Ltd	Heptane, 2-methoxy-2-methyl-	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*
Flammable Liquid Category 3	H226 – Flammable liquid and vapour
Skin Sensitisation 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*
Chronic Aquatic Toxicity Category 3	H412 – Harmful 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.

When used as a fragrance ingredient at maximum concentration of 0.5% in fine fragrances and 0.05% in personal care/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, 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:
  - Flammable Liquid Category 3; H226 – Flammable liquid and vapour
  - Skin Sensitisation Category 1B; 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.

Health Surveillance

- As the notified chemical is a skin sensitiser, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of skin sensitisation.

Safety Data Sheet

- The SDS for imported fragrance formulations containing the notified chemical should include the relevant hazard information.

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:
  - Enclosed, automated processes, where possible
  - Adequate general and local exhaust ventilation

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure when handling the notified chemical during reformulation:
  - Avoid contact with skin
  - Remove all sources of ignition
  - Avoid inhalation of mists, vapours or aerosols

- 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:
  - Protective clothing
  - Impervious gloves
  - Respiratory protection if ventilation measures are insufficient

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

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

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

Disposal

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

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.

- The following precautions should be taken regarding storage of the notified chemical:
  - Store only in original containers
  - Store the containers tightly closed in a cool, dry and well-ventilated place

- Keep away from source of ignition

Emergency procedures

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

Transport and Packaging

- Due to the flammability of the notified chemical, introducers of the chemical should consider their obligations under *Australian Code for the Transport of Dangerous Goods by Road and Rail* (ADG code) (NTC, 2017).

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 final use concentration of the notified chemical exceeds or is intended to exceed 0.5% in fine fragrances and 0.05% in personal care/cosmetic or household products;
- information on the repeated does toxicity of the notified chemical becomes available;

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.

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

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Takasago International (Singapore) Pte Ltd. (ABN: 29 099 666 832)
Level 5, 815 Pacific Highway
CHATSWOOD NSW 2067

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 exempt from publication.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for hydrolysis as a function of pH.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Japan ISHL (2017)
EU REACH (2018)

2. IDENTITY OF CHEMICAL

MARKETING NAME
DAIKON ETHER

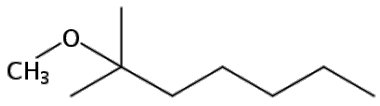
CAS NUMBER
76589-16-7

CHEMICAL NAME
Heptane, 2-methoxy-2-methyl-

OTHER NAME(S)
2-Methoxy-2-methylheptane
NACET10301 (product name used in study reports)

MOLECULAR FORMULA
$C_9H_{20}O$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
144.25 g/mol

ANALYTICAL DATA
Reference spectral data were provided for UV/Vis, FTIR, NMR, GC-MS and GC-FID.

3. COMPOSITION

DEGREE OF PURITY
97%

IDENTIFIED IMPURITIES

Chemical Name	2-Hexene, 5-methoxy-2,5-dimethyl-		
CAS No.	143734-10-5	*Weight %*	2.9
Hazardous Properties	Unknown		

The notified chemical also contains two unidentified impurities (0.2% each). Hazardous properties of these impurities are not known.

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless to pale yellow liquid with special odour

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -80 °C	Measured
Boiling Point	160.5 °C at 101.6 kPa	Measured
Density	793 kg/m^3 at 20 °C	Measured
Vapour Pressure	1.4 kPa at 25 °C	Measured
Water Solubility	0.119 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	Contains no hydrolysable functionalities in environmentally relevant conditions (pH 4–9).
Partition Coefficient (n-octanol/water)	log P_{ow} = 3.7 at 25 °C	Measured
Surface Tension	66.6 mN/m at 20°C (at 90% saturation)	Measured
Adsorption/Desorption	log K_{oc} = 2.14 (MCI method) log K_{oc} = 2.88 (log K_{ow} method)	Calculated by KOCWIN v2.00
Dissociation Constant	Not determined	Contains no dissociable functionalities
Flash Point	45°C (closed cup)	Measured
Flammability	Flammable liquid (Category 3)	Based on flash point
Flammability – contact with water	Not determined	Not expected to react with water forming flammable gases
Flammability – pyrophoric properties	Not determined	Not expected to have pyrophoric properties
Auto-ignition Temperature	210°C at 98.6 kPa	Measured
Explosive Properties	Not determined	Contains no functional groups that imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that imply oxidising properties

DISCUSSION OF PROPERTIES
The notified chemical is expected to be stable under normal conditions of use.

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

Physical hazard classification
Based on the submitted physico-chemical data in the above table, 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*
Flammable Liquid Category 3	H226 – Flammable liquid and vapour

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 at < 5% concentration in liquid fragrance formulations. Neat form of the notified chemical will not be imported.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	0.15	0.15	0.15	0.3	0.6

PORT OF ENTRY
Major cities throughout Australia

TRANSPORTATION AND PACKAGING
The fragrance formulations containing the notified chemical at < 5% concentration will be imported and transported in 200 L drums to reformulation sites. Transportation will be mainly by road.

After reformulation, the finished consumer products containing the notified chemical will be packaged in consumer size containers suitable for retail sale and distributed by road.

USE
The notified chemical will be used as a fragrance ingredient in finished personal care/cosmetic and household products that will be used by consumers and professionals (such as hairdressers, workers in beauty salons and cleaners).

Proposed use concentrations of the notified chemical in finished consumer products are:
- 0.001 – 0.5% in fine fragrances
- 0.0001 – 0.05% in personal care/cosmetic products (e.g. cosmetics, shower gels, shampoos)
- 0.0001 – 0.05% in household products (e.g. laundry detergents)

OPERATION DESCRIPTION

Reformulation
The reformulation processes for incorporating the fragrance formulations containing the notified chemical into end-use products will likely vary depending on the specific type of personal care/cosmetic and household products formulated. The processes may involve both automated and manual procedures including transferring and blending the fragrance formulations containing the notified chemical with other ingredients. Typical blending operations will be highly automated and occur in a fully enclosed/contained environment, followed by automated filling using sealed delivery systems into retail containers of various sizes.

End Use
Personal care/cosmetic products – Depending on the nature of the product, application may be done by hand, sprayed or through the use of an applicator.

Household products – The products may be used in either closed systems with episodes of controlled processes (for example automatic washing machines) or open processes, or manually applied by sponge, mop, spray or brush followed by wiping or 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 storage	1–2 h	50
Mixers	≤ 8 h	240

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Quality control samplers	0.5 h	240
Cleaning and maintenance	≤ 8 h	240
Professional end users	1–8 h	200

EXPOSURE DETAILS

Transport and storage
Transport and storage workers may come into contact with the notified chemical at < 5% concentration only in the unlikely case of an accident involving damage to the containers.

Reformulation
During reformulation, dermal, ocular and possible inhalation exposure of workers to the notified chemical (at < 5% concentration) may occur during weighing, transfer, blending, quality control and cleaning/maintenance of equipment. According to the notifier, exposure is expected to be minimised through the use of general/local exhaust ventilation and enclosed/automated systems and through the use of personal protective equipment (PPE) by workers such as impervious gloves and protective clothing. If exhaust or ventilation measures are insufficient, respiratory protection will be worn.

Professional end use
Exposure to the notified chemical at ≤ 0.5% concentration in finished consumer products may occur in professions where the services provided involve the application of personal care/cosmetic products to clients or the use of household products in the cleaning industry. The principal route of exposure will be dermal, while ocular and inhalation exposure are also possible. Professionals working with the end-products 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 a variety of cosmetic and household consumer products. The principal route of exposure will be dermal, while ocular and inhalation exposures are also possible, particularly if products are applied by spray.

Typical daily systemic exposure to the notified chemical by using the consumer products is shown in the following table. For the purposes of the exposure assessment via the dermal route, Australian use patterns for the various product categories are assumed to be similar to those in Europe (SCCS, 2012; Cadby *et al.*, 2002; ACI, 2010; Loretz *et al.,* 2006). In the absence of empirical dermal absorption information, based on the low molecular weight of the notified chemical (< 500 g/mol), a dermal absorption of 100% is assumed. For the inhalation exposure estimation, a 2-zone approach (Steiling *et al*., 2014; Rothe *et al*., 2011; Earnest, Jr, 2009) is used with assumptions of an adult air inhalation rate of 20 m^3/day (enHealth, 2012) and a conservative chemical inhalation rate of 50%. For calculation purposes, a lifetime average female body weight of 64 kg (enHealth, 2012) is used.

Product type	*Daily systemic exposure (mg/kg bw/day)*
Cosmetic products (dermal exposure)	
Body lotion	0.0611
Face cream	0.0120
Hand cream	0.0169
Fine fragrances	0.0586
Deodorant (non-spray)	0.0117
Shampoo	0.0008
Conditioner	0.0003
Shower gel	0.0015
Hand wash soap	0.0016
Hair styling products	0.0031
Subtotal	**0.1676**
Household products (Indirect dermal exposure – from wearing clothes)	
Laundry liquid	0.0017
Fabric softener	0.0007
Subtotal	**0.0024**

Product type	*Daily systemic exposure (mg/kg bw/day)*
Household exposure (Direct dermal exposure)	
Laundry liquid	0.0000
Dishwashing liquid	0.0001
All-purpose cleaner	0.0011
Subtotal	**0.0012**
Aerosol exposure (Inhalation exposure)	
Hairspray	0.0016
Total	**0.1728**

Based on the calculations, considering the worst case scenario of a consumer exposed simultaneously to all types of products containing the notified chemical at proposed use concentration, the combined internal dose of the notified chemical is estimated to be 0.1728 mg/kg bw/day. It is acknowledged that exposure to the notified chemical from use of other cosmetic and household products that are not listed may occur. However, the combination of the conservative exposure parameters and the aggregate exposure pattern from use of the typical products above is considered adequate to cover these unlisted uses.

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
Skin irritation (*in vitro* EpiSkin Model)	Non-irritating
Eye irritation (*in vitro* BCOP test)	No prediction possible
Eye irritation (*in vitro* EpiOcular Model)	No classification required
Mouse, skin sensitisation – Local lymph node assay	Evidence of sensitisation (EC3 = 71.7%)
Mutagenicity – bacterial reverse mutation	Non mutagenic
Genotoxicity – *in vitro* mammalian cell micronucleus test	Genotoxic with metabolic activation
Genotoxicity – *in vivo* mouse micronucleus test	Non clastogenic

Toxicokinetics, metabolism and distribution

No toxicokinetics data are submitted for the notified chemical. Based on the molecular weight of the notified chemical, the moderate water solubility and the log P_{ow} of 3.7, there is potential for the chemical to cross biological membranes and be absorbed systemically.

Acute toxicity

The notified chemical was found to be of low acute oral toxicity in rats with an LD50 > 2,000 mg/kg bw.

Irritation

In an *in vitro* study using the reconstructed human epidermis EpiSkin Model, the notified chemical was found non-irritating.

In an *in vitro* bovine cornea opacity and permeability (BCOP) test, the notified chemical gave an *in vitro* irritancy score (IVIS) > 3 but < 55. Therefore, no prediction could be made based on the result of this assay. In another *in vitro* eye irritation test using the EpiOcular Model, the notified chemical was determined to not require classification for eye irritation.

Skin sensitisation

The notified chemical elicited a positive response in a mouse local lymph node assay (LLNA). The EC3 was estimated as 71.7%. Given the EC3 value, the notified chemical is not expected to be a strong skin sensitiser, but warrants skin sensitisation classification.

Mutagenicity/Genotoxicity

Negative results were observed for mutagenicity in a bacterial reverse mutation test using *Salmonella typhimurium* strains and an *Escherichia coli* strain, with and without metabolic activation.

In an *in vitro* micronucleus test (OECD 487) using Chinese hamster lung fibroblasts (CHL/IU cells), the notified chemical induced statistically significant increases in micronucleated cells with a dose-dependent response at

concentrations of 214, 255 and 303 µg/mL, in the presence of metabolic activation. No increase in micronucleated cells was observed when tested without metabolic activation up to 720 µg/mL.

In an *in vivo* micronucleus test (OECD TG 474), the notified chemical administered by oral gavage to mice at concentrations up to 2,000 mg/kg bw per day for 2 days did not induce clastogenic effects in bone marrow erythrocytes. However, there was no indication of the test material reaching bone marrow of treated mice, reducing the validity of the negative results reported.

The notified chemical showed no structural alerts for genotoxicity in quantitative structure activity relationship modelling (QSAR Toolbox 4.2). A similar chemical butane, 2-methoxy-2-methyl- (CAS No. 994-05-8) assessed in the European Union showed comparable results for genotoxicity when tested *in vitro* and *in vivo*. Formaldehyde release from metabolism was hypothesised to be the probable cause for the *in vitro* chromosome aberrations (EU RAR, 2006). The notified chemical is likely to have similar metabolic properties to this chemical. However, QSAR Toolbox simulator did not indicate that the notified chemical would likely release formaldehyde from skin metabolism (QSAR Toolbox 4.2).

Based on the available information, the notified chemical is not expected to be genotoxic.

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 Sensitisation Category 1B	H317 – May cause an allergic skin reaction

6.3. Human Health Risk Characterisation
The notified chemical is a skin sensitiser with an EC3 of 71.7% derived from a mouse LLNA, indicative of weak skin sensitisation potential. Toxicity of the notified chemical upon repeated or prolonged dermal exposure is unknown. As the notified chemical will be used at very low concentrations (≤ 0.5%) in personal care/cosmetic or household products, significant systemic exposure is not expected.

6.3.1. Occupational Health and Safety

Reformulation
The notified chemical will be imported as a component at < 5% concentration in liquid fragrance formulations. During reformulation, worker exposure will be limited through the use of engineering controls (such as enclosed/automated systems and local exhaust ventilation) and appropriate PPE (skin/eye protection and respiratory protection if inhalation is expected), as anticipated by the notifier.

Professional end-use
Workers involved in professions may be exposed to the notified chemical at ≤ 0.5% concentration where the services provided involve the application of personal care/cosmetic products containing the notified chemical to clients (e.g. by hairdressers and beauty salon workers) or the use of household products in the cleaning industry (e.g. by cleaners). Such professionals may use PPE such as gloves, glasses, face masks and protective clothing to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, the risk to such workers is expected to be of a similar or lesser extent than that for consumers using the various products containing the notified chemical.

Overall, 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.

6.3.2. Public Health
Members of the public are expected to be repeatedly exposed to the notified chemical during the use of personal care/cosmetic products and household products containing the notified chemical up to 0.5% concentration in fine fragrances and up to 0.05% in other cosmetic and personal care products.

Skin Sensitisation
Quantitative risk assessment for skin sensitisation (Api *et al.,* 2008; Cadby *et al.,* 2002; and RIVM, 2010) was conducted using fine fragrance as an example product that may contain the notified chemical at 0.5%

concentration (worst case scenario). The Consumer Exposure Level (CEL) for the notified chemical is estimated to be 18.75 µg/cm^2/day. When tested in an LLNA study, the notified chemical was a skin sensitiser with an EC3 value of 71.7%. Consideration of the study details and application of appropriate safety factors allowed the derivation of an Acceptable Exposure Level (AEL) of 47.41 µg/cm^2/day. In this instance, the factors employed included an interspecies factor (3), intraspecies factor (10), a matrix factor (3.16), use/time factor (3.16) and database factor (1), giving an overall safety factor of > 300.

As the CEL is estimated to be less than the AEL, the risk to the public of induction of skin sensitisation that is associated with the use of fine fragrances 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 (SCCS, 2018) has not been conducted.

Repeated or Prolonged Exposure
The repeated dose toxicity effects of the notified chemical have not been determined. Systemic dermal exposure is expected to be limited by the low concentration of the notified chemical in the end use products. In a worst case scenario for a consumer using simultaneously all types of typical end use products, the internal dose of the notified chemical may reach 0.1728 mg/kg bw/day (see Section 6.1.2.)

Based on the information available, the risk to the public associated with the use of the notified chemical at maximum concentration of 0.5% in fine fragrances and 0.05% in personal care/cosmetic products and household products is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The notified chemical will be imported into Australia as a component of fragrance mixtures, for reformulation into finished personal care/cosmetic and household products. In general, the reformulation processes are expected to involve automated blending operation in an enclosed environment, followed by automated filling of the finished products into end-use containers. Wastewater from reformulation equipment cleaning containing the notified chemical will either be released to sewers or disposed of to landfill according to local government regulations. Release of the notified chemical to the environment in the event of accidental spills or leaks during reformulation, storage and transport is expected to be collected for disposal, in accordance with local government regulations.

RELEASE OF CHEMICAL FROM USE
The majority of the notified chemical is expected to be released to sewers across Australia as a result of its use in personal care/cosmetic and household products, which are washed off hair and skin of consumers as well as from cleaning activities.

RELEASE OF CHEMICAL FROM DISPOSAL
Residues of the notified chemical in empty end-use 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 the containers are rinsed before recycling through an approved waste management facility.

7.1.2. Environmental Fate
Following its use in personal care/cosmetic and household products, the majority of the notified chemical is expected to enter sewers across Australia. Based on its high vapour pressure (1.4 kPa) and moderate water solubility (0.119 g/L), the notified chemical is expected to be highly volatile from water (Henrys Law constant; LogH = 3.230) and partition from water to air. However, in air the notified chemical is not expected to persist as the half-life of the notified chemical in air is calculated to be around 12.9 hours, based on reactions with hydroxyl radicals (US EPA, 2012; calculated using AOPWIN v1.92). Based on its moderate water solubility and its log P_{ow} (3.7), the notified chemical is expected to present in both water and sludge at sewage treatment plants (STPs). The ready biodegradation test conducted on the notified chemical shows that it is not readily biodegradable (no degradation over 28 days in OECD 301C test). For details of the environmental fate studies,

please refer to Appendix C. Therefore, a proportion of the notified chemical may remain in STP effluent and potentially be released to surface waters nationwide. A proportion of the notified chemical may be applied to land when effluent is used for irrigation or when sewage sludge is used for soil remediation, or disposed of to landfill. The notified chemical residues in sludge, landfill and soils are expected to have medium mobility based on its calculated soil adsorption coefficient (log K_{oc} = 2.14 to 2.88). In the aquatic and soil compartments, the notified chemical is expected to eventually degrade through biotic and abiotic processes to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated to assume the worst case scenario with 100% release of the notified chemical into sewer systems nationwide over 365 days per annum. It is also assumed under the worst-case scenario that there is no removal of the notified chemical during sewage treatment processes. The resultant PEC in sewage effluent on a nationwide basis is estimated as follows:

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	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	0	%
Daily effluent production:	4,877	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.56	µg/L
PEC - Ocean:	0.06	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.56 µg/L may potentially result in a soil concentration of approximately 3.74 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 18.7 µg/kg and 37.4 µg/kg, respectively.

7.2. Environmental Effects Assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Daphnia Toxicity	48 h EC50 = 24 mg/L	Harmful to aquatic invertebrates
Algal Toxicity	72 h EC50 = 23 mg/L	Harmful to algae

Under the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), the notified chemical is expected to be harmful to aquatic invertebrates and alga. Therefore, the notified chemical is formally classified as "Acute Category 3; Harmful to aquatic life" under the GHS. Based on the acute toxicity and lack of ready biodegradation, the notified chemical is formally classified as "Chronic Category 3; Harmful to aquatic life with long lasting effects" under the GHS (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

The conservative predicted no-effects concentration (PNEC) has been calculated based on the endpoint for algae as shown in the table below. A conservative safety factor of 500 was used given the acute endpoints for only two trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
72 h EC50 for algae	23	mg/L
Assessment Factor	500	
Mitigation Factor	1	

PNEC	46	µg/L

7.3. Environmental Risk Assessment

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

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.56	46	**0.012**
Q - Ocean	0.06	46	**0.001**

The risk quotient for discharge of effluents containing the notified chemical to the aquatic environment indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations based on its annual importation quantity. Therefore, on the basis of the PEC/PNEC ratio, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point < -80°C (< 193 K)

Method	EC Guideline A.1. Melting/Freezing Temperature. March 04, 2016 OECD Guideline 102. Melting Point / Melting Range. July 27, 1995 EPA Product Properties Test Guideline OPPTS 830.7200: Melting Point/Melting Range. March 1998
Remarks	Differential scanning calorimetry (DSC) was used. Crystallisation and melting were not observed in the temperature range from -90 to 400 °C. Additional samples were placed overnight at -19 and –80 °C, both resulting in liquid forms. The freezing point was therefore determined to be < -80°C.
Test Facility	CRL (2018a)

Boiling Point 160.5°C (433.6 K) at 101.6 ± 1.2 kPa

Method	EC Guideline A.2. Boiling Temperature. March 04, 2016 OECD Guideline 103. Boiling Point. July 27, 1995 EPA Product Properties Test Guideline OPPTS 830.7220: Boiling Point/Boiling Range. August 1996
Remarks	The boiling point was measured using DSC. Preliminary study A sample of 3.48 g was heated at a rate of 20°C /min to 160°C. The weight of the sample decreased significantly from 120°C onward, with 70% loss at 160°C. Main study Four experiments were conducted, resulting in the following boiling temperature values: 160.685°C, 161.038°C, 153.363°C and 160.313°C. Because of higher heating rate in Experiment 2 and complete evaporation in Experiment 3, the boiling temperature of the test item was determined as the mean value of Experiments 1 and 4: 160.5°C.
Test Facility	CRL (2018a)

Density 793 kg/m^3 at 20 °C

Method	EC Guideline A.3. Relative Density. March 04, 2016 OECD Guideline 109. Density of Liquids and Solids. October 2, 2012 EPA Product Properties Test Guideline OPPTS 830.7300: Density/Relative Density/ Bulk Density. June 2002
Remarks	Density and relative density of the test item were measured using a pycnometer, at 20°C. Two experiments were conducted. The density of the test item was determined as the mean value of both experiments.
Test Facility	CRL (2018a)

Vapour Pressure 0.96 kPa at 20 °C
1.4 kPa at 25 °C

Method	EC Guideline A.4. Vapour Pressure. March 04, 2016 OECD Guideline104. Vapour Pressure. March 23, 2006 EPA Product Properties Test Guideline OPPTS 830.7950: Vapour pressure. August 1996
Remarks	The vapour pressure of the test item was determined by the isothermal thermogravimetric effusion method.
Test Facility	CRL (2018a)

Water Solubility 0.119 g/L at 20 °C

Method	OECD TG 105 Water Solubility EC Council Regulation No 440/2008 A.6 Water Solubility
Remarks	Flask Method
Test Facility	CRL (2018b)

Partition Coefficient (n-octanol/water) log P_{ow} = 3.7.at 25 °C

Method	OECD TG 117 Partition Coefficient (n-octanol/water).
Remarks	HPLC Method
Test Facility	CERI (2017a)

Surface Tension 66.6 mN/m at 20°C

Method	EC Guideline A.5. Surface Tension. March 04, 2016 OECD Guideline 115. Surface Tension of Aqueous Solutions. July 27, 1995
Remarks	Concentration: 90% saturation in water at 20.7 ± 0.2 °C Five measurements were conducted until a constant value on the surface tension was reached, providing the following values: 65.6, 65.8, 66.0, 65.5 and 65.7 mN/m with mean value at 65.7 mN/m. Based on Harkins-Jordan, the corrected value was calculated as 66.6 mN/m at 20 °C with a calibration factor (Φ_b) of 1.02.
Test Facility	CRL (2018a)

Flash Point 45 °C

Method	EC Guideline A.9. Flash-point. March 04, 2016 UN no. ST/SG/AC.10/11/Rev.6 Paragraph 32.4.1: Non-Viscous Flammable Liquids. 2015 ASTM D93. Standard Test Methods for Flash Point by Pensky-Martens Closed Cup Tester. December 10, 2002 ASTM D7094. Standard Test Method for Flash Point by Modified Continuously Closed Cup (MCCCFP) Tester. 2012 ISO Guide 2719. Determination of Flash Point - Pensky-Martens Closed Cup Method. 2002 ISO Guide 3679. Determination of Flash Point - Rapid Equilibrium Closed Cup Method. 2004
Remarks	The test was conducted using the closed cup method. <u>Preliminary study</u> Starting at 25 °C, the test cup was heated at a rate of 5 °C/minute, ignition attempts were made for every 2 °C temperature rise. The flash point was estimated to be 45 °C. <u>Main study</u> Two tests were performed. Starting at 22 °C, the test cup was heated at a rate of 5 °C/minute, ignition attempts were made for every 1 °C temperature rise. In both tests, the flash point was found to be 45 °C.
Test Facility	CRL (2018a)

Autoignition Temperature 210 °C at 98.6 kPa

Method	EC Guideline A.15. Auto-Ignition Temperature (Liquids and Gases). March 04, 2016 DIN Guide 51794: Determining the Ignition Temperature of Petroleum Products. May 2003
Remarks	<u>Preliminary study</u> Starting at 200 °C, for every 20 °C temperature rise, the test item was introduced into the test vessel until ignition was first observed (i.e. at 240 °C). Starting at 250 °C, for every 5 °C decrease, the test item was tested until no ignition had been observed. The auto ignition temperature was estimated to be 235 °C. <u>Main study</u> Three tests were conducted, resulting in the following minimum auto ignition temperatures: 214°C, 219 °C and 217°C. The lowest temperature was rounded to the nearest multiple of 5°C (i.e. 210 °C).
Test Facility	CRL (2018a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method
Species/Strain	Rat/Wistar [Crl: WI (Han)]
Vehicle	None
Remarks - Method	The toxicity of the test item was assessed by stepwise treatment of groups of 3 animals. The first group was treated with a dose of 2,000 mg/kg bw. Based on the results, an additional group was treated with 2,000 mg/kg bw.

RESULTS

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

LD50	> 2,000 mg/kg bw
Signs of Toxicity	One rat was terminated in extremis on day 2. Lethargy, flat or hunched posture, uncoordinated movements, laboured respiration, piloerection, salivation, watery discharge from the right eye and ptosis were noted for this animal before termination. The other animals survived the 14-day observation period. Signs of toxicity included lethargy, hunched posture, uncoordinated movements, piloerection and/or salivation between days 1 and 3.
Effects in Organs	No abnormalities were noted at macroscopic post mortem examination.
Remarks - Results	No major deviations of protocol were noted.
CONCLUSION	The notified chemical is of low acute toxicity via the oral route.
TEST FACILITY	CRL (2018c)

B.2. Irritation – skin (*in vitro* reconstructed human Epidermis test)

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 439 *In vitro* Skin Irritation: Reconstructed Human Epidermis Test Method
Vehicle	None
Negative control	Phosphate buffered saline (PBS)
Positive control	5% Sodium dodecyl sulfate (SDS)
Remarks - Method	The test item was checked before the study for possible colour interference and direct MTT reduction.

RESULTS

Test Material	*Mean OD_{570} of Triplicate Tissues*	*Relative Mean Viability (%)*	*SD of Relative Mean Viability*
Negative control	0.88	100	1
Test substance	0.757	86	3.4
Positive control	0.137	16	8

OD = optical density; SD = standard deviation

Remarks - Results	The results showed that the notified chemical did not interfere with the MTT reaction. The relative mean viability of the tissues treated with the

notified chemical was > 50%.

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

TEST FACILITY CRL (2018d)

B.3. Irritation – eye (*in vitro* BCOP)

TEST SUBSTANCE Notified chemical

METHOD OECD TG 437 Bovine Corneal Opacity and Permeability Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage

Vehicle	None
Negative control	Physiological saline
Positive control	Ethanol
Remarks - Method	The test item was checked before the study for possible colour interference and direct MTT reduction.

RESULTS

Test Material	*Mean Opacities of Triplicate Tissues*	*Mean Permeabilities of Triplicate Tissues*	*IVIS*
Negative control	0.3	0.005	0.4
Test substance	5.9	0.137	7.9
Positive control	17	2	47

IVIS = *in vitro* irritancy score

Remarks - Results The results showed that the notified chemical did not interfere with the MTT reaction. The IVIS for the test substance was 7.9, indicating no prediction is possible for hazard classification (IVIS > 3 and ≤ 55).

CONCLUSION No prediction can be made.

TEST FACILITY CRL (2018e)

B.4. Irritation – eye (*in vitro* reconstructed human EpiOcular™ model)

TEST SUBSTANCE Notified chemical

METHOD OECD Guideline 492 Reconstructed Human EpiOcular™ Model Test Method for Identifying Chemicals Not Requiring Classification and Labelling for Eye Irritation or Serious Eye Damage

Vehicle	None
Negative control	Sterile Milli-Q water
Positive control	Methyl acetate
Remarks - Method	The test item was checked before the study for possible colour interference and direct MTT reduction.

RESULTS

Test Material	*Mean OD_{570} of Duplicate Tissues*	*Relative Mean Viability (%)*
Negative Control	1.613	100
Test Substance	1.101	68
Positive Control	0.539	33

OD = optical density

Remarks - Results The results showed that the notified chemical did not interfere with the MTT reaction. The relative mean viability of the tissues treated with the notified chemical was > 60%.

CONCLUSION	The notified chemical does not require classification for eye irritation or serious eye damage.
TEST FACILITY	CRL (2018f)

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 J
Vehicle	Ethanol/diethylphthalate (1:3 v/v)
Preliminary study	Yes
Positive control	α-Hexylcinnamaldehyde (HCA)
Remarks - Method	No major deviation of protocol was noted.

RESULTS

Concentration (% w/w)	*Number and Sex of Animals*	*Proliferative Response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance			
0 (vehicle control)	5F	769	1.0
25	5F	1,132	1.5
50	5F	1,518	2.0
100	5F	3,322	4.3
Positive Control			
25	5F	2,522	3.3

EC3	71.7%
Remarks - Results	No irritation or signs of systemic toxicity were observed in any of the test animals. No macroscopic abnormalities of the lymph nodes were noted for any of the animals.
CONCLUSION	There was evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.
TEST FACILITY	CRL (2017a)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test
Species/Strain	*Salmonella typhimurium*: TA1535, TA1537, TA98, TA100 *Escherichia coli*: WP2uvrA
Metabolic Activation System	S9 mix prepared from phenobarbital and 5,6-benzoflavone induced rat liver homogenate
Concentration Range in Main Test	a) With metabolic activation: 9.77–313 µg/plate b) Without metabolic activation: 9.77–313 µg/plate
Vehicle	DMSO
Remarks - Method	No major deviation of protocol was noted.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* Cytotoxicity in Preliminary Test	Cytotoxicity in Main Test	Precipitation	Genotoxic Effect
Absent				
Test 1	≥ 313	≥ 156	Not observed	Negative
Test 2	-	≥ 156	Not observed	Negative

Present				
Test 1	≥ 313	≥ 313	Not observed	Negative
Test 2	-	≥ 313	Not observed	Negative

Remarks - Results The test substance did not induce significant increases in the number of revertant colonies in the test strains when compared with the vehicle control.

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

TEST FACILITY UBE (2017a)

B.7. Genotoxicity – *in vitro* mammalian cell micronucleus test

TEST SUBSTANCE Notified chemical

METHOD OECD TG 487 In Vitro Mammalian Cell Micronucleus Test
Species/Strain Chinese Hamster
Cell Type/Cell Line Lung fibroblast/CHL/IU
Metabolic Activation System S9 mix prepared from phenobarbital and 5,6-benzoflavone induced rat liver homogenate
Vehicle Acetone
Positive Control Mitomycin C (-S9 mix)/ Benzo[a]pyrene (+S9 mix)
Remarks - Method No major deviation of protocol was noted.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	303, 360, 428, 509*, 605*, 720*	6 h	24 h
Test 2	127, 151, 180, 214, 255, 303, 360, 428, 509, 605	24 h	24 h
Test 3	160, 180, 202, 227, 255, 286, 321, 360	24 h	24 h
Present			
Test 1	151, 180, 214*, 255*, 303*, 360	6 h	24 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	≥ 720	≥ 720	None	Negative
Test 2	≥ 720	≥ 360	None	Not tested
Test 3	-	≥ 360	None	Not tested
Present				
Test 1	≥ 360	≥ 303	None	Positive

Remarks - Results Significant increases in micronucleated cells were observed with a dose response at 214, 255 and 303 µg/mL resulting in increases of 5.7%, 4.7% and 5.8% respectively in 6 h treatment in the presence of S9 mix.

No significant increase in micronucleated cells was observed in the 6 h treatment without metabolic activation, up to 720 µg/mL.

Observations were not carried out for 24 h treatment since positive results were confirmed in the 6 h treatment.

CONCLUSION The notified chemical was considered clastogenic to CHL/IU cells treated *in vitro* with metabolic activation.

TEST FACILITY UBE (2017b)

B.8. Genotoxicity – *in vivo* mammalian erythrocyte micronucleus test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 474 Mammalian Erythrocyte Micronucleus Test
Species/Strain	Mice/ Crl: CD1 (ICR)
Route of Administration	Oral gavage
Vehicle	Corn oil
Positive Control	Mitomycin C (single intraperitoneal injection)
Remarks - Method	The notified chemical was administered twice by gavage, 24 hours apart. Animals were euthanized 24 hours following the second administration. No major deviation of protocol was recorded.

Group	*Number and Sex of Animals*	*Concentration (mg/kg bw)*	*Sacrifice Time (hours)*
I (vehicle control)	5M	0	24
II (low dose)	5M	500	24
III (mid dose)	5M	1,000	24
IV (high dose)	5M	2,000	24
V (positive control, M)	5M	2	24

M = mitomycin C

RESULTS	
General Toxicity Signs	500 mg/kg: piloerection (1/5), incomplete eyelid opening (1/5) 1,000 mg/kg: piloerection(2/5), ataxic gait (3/5) 2,000 mg/kg: piloerection (3/5), incomplete eyelid opening (2/5), ataxic gait (5/5), decreased motor activity (4/5)
Genotoxic Effects	No significant difference was observed in micronucleated polychromatic erythrocytes (MNPCE) frequencies between control and treated groups.
Remarks - Results	The incidence of MNPCE was 0.174% in the vehicle control group. For the treatment groups, the incidences of MNPCE ranged from 0.148% to 0.168% with no clear dose response and did not exceed the upper limit of the vehicle control. In the positive control group, the incidence of MNPCE was 2.794%, exceeding the upper limit of the vehicle control. The test substance was not identified in plasma of the treated mice. There was no evidence of the test material reaching the bone marrow of orally dosed mice.
CONCLUSION	The notified chemical was reported as not clastogenic under the conditions of this *in vivo* mammalian erythrocyte micronucleus test.
TEST FACILITY	DIMS (2017)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 C Ready Biodegradability: Modified MITI Test (I)
Inoculum	Mixed sludge from 10 locations from rivers, lakes, inland sea and STPs
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Biochemical oxygen demand (BOD) by oxygen consumption measuring apparatus, and test substance by Gas Chromatography - Flame Ionisation Detector (GC - FID)
Remarks - Method	No major deviations from the test guidelines were reported. A 100 mg/L test solution was prepared by directly adding the test item to the test water.

RESULTS

Test Substance		*Aniline*	
Day	*% Degradation*	*Day*	*% Degradation*
7	-1	7	75
14	-2	14	88
21	-2	21	93
28	-2	28	96

Remarks - Results	All validity criteria for the test were satisfied. No degradation of the notified chemical was observed after 28 days based on GC and BOD analyses.
CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	CERI (2017b)

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 - Static
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	Approximately 180 mg $CaCO_3$/L
Analytical Monitoring	GC - FID
Remarks - Method	A final test was performed based on the results from a preceding combined limit/range-finding test. No major deviations from the test guidelines were reported. A loading nominal rate of 100 mg/L of the test item was prepared and stirred for three days and settled for one hour. The Water Accommodated Fraction (WAF) was siphoned and used as the highest test concentration. Lower test concentrations were prepared by subsequent dilutions of the highest test concentration. The test substance in test water was analysed by GC-FID at the beginning and the end of the test. A reference test with potassium dichromate was also conducted prior to the current study.

RESULTS

Measured concentration (mg/L)		*Number of D. magna*	*Number Immobilised*	
Initial	*End of test*		*24 h*	*48 h*
Control	Control	20	0	0
5.47	5.27	20	0	0
11.5	10.9	20	0	0
21.8	17.1	20	1	3
33.8	37.8	20	14	20
68.9	68.7	20	15	20

LC50	24 mg/L nominal concentration at 48 hours (95% confidence interval between 22 and 26 mg/L, calculated by the Spearman-Karber method)
Remarks - Results	All validity criteria for the test were satisfied. Dissolved oxygen concentration during the test was ≥ 8.4 mg/L at 20°C (≥ 92%, USGS, 2011). The actual responses in the reference test were within the ranges of the expected responses at the different potassium dichromate concentrations. Therefore, the sensitivity of this batch of *D. magna* was in agreement with the historical data collected at the test facility.
CONCLUSION	The notified chemical is harmful to aquatic invertebrates.
TEST FACILITY	CRL (2018g)

C.2.2. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test
Species	*Raphidocelis subcapitata* (formerly known as *Pseudokirchneriella subcapitata*)
Exposure Period	72 hours
Concentration Range	Actual average: 0.39, 1.1, 4.0, 4.3, 13, 42 mg/L
Auxiliary Solvent	None
Water Hardness	Not provided
Analytical Monitoring	GC - FID
Remarks - Method	A final test was performed based on a preceding range-finding test with no major deviations from the test guidelines. A nominal loading rate of 100 mg/L of the test item was prepared and stirred for three days and settled for one hour. The Water Accommodated Fraction (WAF) was siphoned and used as the highest test concentration. Lower test concentrations were prepared by subsequent dilutions of the highest test concentration. The test substance in test water was analysed by GC-FID at the beginning and the end of the test. A reference test with potassium dichromate was also conducted prior to the current study.

RESULTS

Biomass		*Growth*	
EC50 (mg/L at 72 h)	*NOEC (mg/L)*	*EC50 (mg/L at 72 h)*	*NOEC (mg/L)*
8.0 (95% CL of 7.3 – 8.7)	1.1	23 (95% CL of 23-24)	4.0

Remarks - Results	All validity criteria for the test were satisfied. The cell density in the control increased 214 times after 72 hours. The observed 72 h ECr50 in the reference test was 0.86 mg/L which was within the historical ranges collected at the test facility.
CONCLUSION	The test substance is harmful to algae.
TEST FACILITY	CRL (2018h)

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

CERI (2017a) Measurement of 1-Octanol/Water Partition Coefficient for DAIKON ETHER (Study No. 85129, May 2017) Japan, Chemical Evaluation and Research Institute (CERI) (Unpublished report submitted by the notifier)

CERI (2017b) Biodegradation Study of DAIKON ETHER (Study No. 16363, April 2017) Japan, Chemical Evaluation and Research Institute (CERI) (Unpublished report submitted by the notifier)

CERI (2017c) A 48-hour Acute Immobilization Study in Daphnia magna (Study No. 97796, June 2017) Chemicals Evaluation and Research Institute, Japan, Kurume, Fukuoka, Japan (Unpublished report submitted by notifier)

CRL (2017a) Assessment of Skin Sensitization to DAIKON ETHER in the Mouse (Local Lymph Node Assay) (Study No. 517010, March 2017) Charles River Laboratories Den Bosch BV, The Netherlands (Unpublished report submitted by notifier)

CRL (2018a) Determination of Physico-Chemical Properties of DAIKON ETHER (Study No. 20135858, April 2018) The Netherlands, Charles River Laboratories Den Bosch BV (Unpublished report submitted by the notifier)

CRL (2018b) Determination of Physico-Chemical Properties of DAIKON ETHER (Study No. 20135859, April 2018) The Netherlands, Charles River Laboratories Den Bosch BV (Unpublished report submitted by the notifier)

CRL (2018c) An Acute Study of DAIKON ETHER by Oral Gavage in Rat (Acute Toxic Class Method) (Study No. 20135863, January 2018) Charles River Laboratories Den Bosch BV, The Netherlands (Unpublished report submitted by notifier)

CRL (2018d) In vitro Skin Irritation Test with DAIKON ETHER using a Human Skin Model (Study No. 20135860, February 2018) Charles River Laboratories Den Bosch BV, The Netherlands (Unpublished report submitted by notifier)

CRL (2018e) Evaluation of the Eye Hazard Potential of DAIKON ETHER using the Bovine Corneal Opacity and Permeability Test (BCOP Test) (Study No. 20135862, January 2018) Charles River Laboratories Den Bosch BV, The Netherlands (Unpublished report submitted by notifier)

CRL (2018f) Evaluation of the Eye Hazard Potential with DAIKON ETHER using the EpiOcular™ Cornea Epithelial Model (Study No. 20146105, May 2018) Charles River Laboratories Den Bosch BV, The Netherlands (Unpublished report submitted by notifier)

CRL (2018g) Acute Toxicity Study in Daphnia magna with DAIKON ETHER (Static) (Study No. 20135864, May 2018) Charles River Laboratories Den Bosch BV, The Netherlands (Unpublished report submitted by notifier)

CRL (2018h) Fresh Water Algal Growth Inhibition Test with DAIKON ETHER (Study No. 20135865, May 2018) Charles River Laboratories Den Bosch BV, The Netherlands (Unpublished report submitted by notifier)

DIMS (2017) Micronucleus Test of DAIKON ETHER and NACET10634 in Mice (Study No. 17204, October 2017) DIMS Institute of Medical Science, Inc., Japan (Unpublished report submitted by notifier)

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

European Union Risk Assessment Report (2006). 2-Methoxy-2-methylbutane (TAME) CAS No: 994-05-8 EINECS No: 213-611-4 Risk Assessment. Finnish Environment Institute 2006

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

NTC (2017) Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), Edition 7.5, National Transport Commission, Commonwealth of Australia

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

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

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

Scientific Committee on Consumer Safety (SCCS) 2018. OPINION ON Skin Sensitisation Quantitative Risk Assessment for Fragrance Ingredients (QRA2) Submission I. Adopted 30 July 2018

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

SWA (2012) Code of Practice: Managing Risks of Hazardous Chemicals in the Workplace, Safe Work Australia, https://www.safeworkaustralia.gov.au/doc/model-code-practice-managing-risks-hazardous-chemicals-workplace

SWA (2015) Code of Practice: Spray Painting and Powder Coating, Safe Work Australia, https://www.safeworkaustralia.gov.au/doc/model-code-practice-spray-painting-and-powder-coating.

UBE (2017a) Bacterial Reverse Mutation Test of DAIKON ETHER (Study No. USA-R-16378, February, 2017) UBE Scientific Analysis Laboratory, Inc.,Yamaguchi., Japan (Unpublished report submitted by notifier)

UBE (2017b) In vitro Mammalian Cell Micronucleus Test (Study No. USA-R-16380, April 2017) Scientific Analysis Laboratory, Inc.,Yamaguchi, Japan (Unpublished report submitted by notifier)

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 (2012) Estimation Programs Interface (EPI) SuiteTM for Microsoft® Windows, v 4.10. United States Environmental Protection Agency. Washington DC, USA.

USGS (2011) U.S. Geological Survey, Change to solubility equations for oxygen in water: Office of Water Quality Technical Memorandum 2011.03, accessed https://water.usgs.gov/software/DOTABLES/ v 3.5, 8 January 2018