File No: LTD/2033

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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Alkenes, C_{12-14}, hydroformylation products, distn. lights

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/2033	Symrise Pty Ltd	Alkenes, C_{12-14}, hydroformylation products, distn. lights	Yes	< 1 tonne per annum	Fragrance ingredient

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard classification	*Hazard statement*
Skin irritation (Category 2)	H315 – Causes skin irritation
Skin sensitisation (Category 1)	H317 – May cause an allergic skin reaction

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 in the proposed manner, the notified chemical is not considered to pose an unreasonable risk to public health.

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

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Skin Irritation Category 2: H315 – Causes skin irritation
  - Skin Sensitisation Category 1: H317 – May cause an allergic skin reaction

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

Health Surveillance

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

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical during reformulation processes:
  - Enclosed, automated processes, where possible
  - Local exhaust ventilation

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

- 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:
  - Protective clothing
  - Gloves
  - Safety glasses or goggles

  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.

Emergency procedures

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

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
- the importation volume exceeds one tonne per annum notified chemical;
- the concentration of the notified chemical exceeds 0.1% in fine fragrances or household products and 0.04% in other cosmetic products;

or

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

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

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

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

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

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

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

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for all physical and chemical properties.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
Previous permit (NICNAS)

NOTIFICATION IN OTHER COUNTRIES
Philippines (2016)
EU (2015)
USA (2007)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Linolal

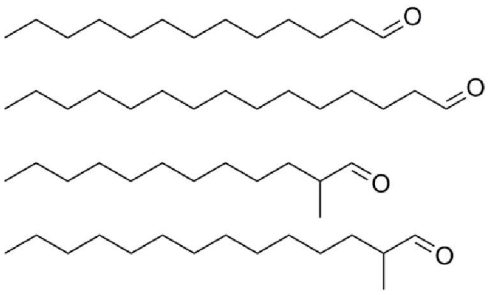
CAS NUMBER
93821-14-8

CHEMICAL NAME
Alkenes, C_{12-14}, hydroformylation products, distn. lights

MOLECULAR FORMULA
Unspecified

STRUCTURAL FORMULA
Unspecified

The notified chemical is a substance of unknown or variable composition, complex reaction products or biological materials (UVCB) and may include following as major components (to a total of ~85 – 90% by weight):



(Structure provided by the notifier)

MOLECULAR WEIGHT
198.34 – 226.40 g/mol

ANALYTICAL DATA

METHOD	^{1}H NMR
Remarks	Consistent with the chemical structure
TEST FACILITY	Symrise (2006)

METHOD	^{13}C NMR
Remarks	Consistent with the chemical structure
TEST FACILITY	Symrise (2006)

METHOD	FTIR
Remarks	Major peaks at 3000 – 2800, ~1750 cm^{-1}, consistent with the chemical structure
TEST FACILITY	Symrise (2006)

METHOD	GC-MS
Remarks	Consistent with the chemical structure
TEST FACILITY	Symrise (2006)

METHOD	UV-VIS
Remarks	No absorbance observed, solvent = ethanol
TEST FACILITY	Symrise (2006)

3. COMPOSITION

DEGREE OF PURITY
> 99%

HAZARDOUS IMPURITIES
None identified

NON HAZARDOUS IMPURITIES (> 1% BY WEIGHT)
None

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: clear colourless liquid

Property	Value	Data Source/Justification
Melting Point	-9 °C	SDS
Boiling Point	263 – 286 °C at 101.3 kPa	SDS
Density	825 – 835 kg/m^3 at 20 °C	SDS
Vapour Pressure	0.3 kPa at 20 °C	SDS
Water Solubility	0.002 g/L at 20 °C	SDS
Hydrolysis as a Function of pH	Not determined	Contains no hydrolysable functionality
Partition Coefficient (n-octanol/water)	log P_{ow} = 5.2 – 6.2	Estimated by KOWWIN v.1.68 (US EPA, 2012)
Adsorption/Desorption	log K_{oc} = 2.5 – 3.1 (MCI method) log K_{oc} = 3.5 – 4.1 (log P_{ow} method)	Estimated by KOCWIN v.2.00 (US EPA, 2012)
Dissociation Constant	Not determined	Contains no dissociable functionality
Flash Point	112 °C	SDS
Flammability	Combustible liquid[#]	SDS
Autoignition Temperature	215 °C at 100.1 kPa	SDS
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties

Property	Value	Data Source/Justification
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties

[#] Based on *Australian Standard AS1940 definitions*

DISCUSSION OF PROPERTIES
No details of tests on physical and chemical properties were submitted.

Reactivity
The notified chemical is expected to be stable under normal conditions of use. However, the notified chemical contains potentially reactive aldehyde functional groups.

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 122 ºC which is greater than 93 °C but less than its boiling point (~263 ºC). Based on *Australian Standard AS1940* definitions for combustible liquid, the notified chemical may be considered as a Class C2 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. The notified chemical will be imported as a fragrance ingredient in finished consumer products at ≤ 0.1% concentration. It may also be imported in neat form (at 100% concentration), in fragrance preparations at ≤ 4% concentration, or in a solution at ≤ 10% concentration for local 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

IDENTITY OF RECIPIENTS
Symrise Pty Ltd

TRANSPORTATION AND PACKAGING
The fragrance preparations or the solution containing the notified chemical at ≤ 4% or ≤ 10% concentration respectively will be mostly imported in lacquered metal drums of 30 L or 216 L size, or in plastic canisters of 30 L size. The notified chemical introduced in neat form will be imported in sealed 30 L lacquered steel cans.

Finished consumer products containing the notified chemical at ≤ 0.1 % concentration will be packaged in containers suitable for retail sales.

The notified chemical and products containing the notified chemical will be transported by road and rail for distribution.

USE
The notified chemical will be used as a fragrance ingredient in cosmetic and household products. The proposed maximum use concentration of the notified chemical in various consumer products will be:

Finished Consumer Product	*Maximum Final Concentration of the Notified Chemical (%)*
Fine fragrance	0.1
Other cosmetic products	0.04
Household cleaning products	0.1

OPERATION DESCRIPTION

Reformulation
Reformulation of fragrance preparations containing the notified chemical will occur at the customer sites. The reformulation processes will likely vary depending on the specific type of the cosmetic and household products, but will most likely be carried out in enclosed and automated systems. Typical reformulation processes will involve blending with other ingredients at measured doses into a variety of products, including perfumes, cosmetics, toiletries, detergents, soaps and other household products. The finished consumer products are then packaged into suitable sizes and transported to retail outlets for sale to the public.

End Use
Finished household cleaning products containing the notified chemical at ≤ 0.1 % concentration may be used by consumers and professional cleaners. The cleaning products will be generally applied with a cloth, sponge, mop or brush, or by spray followed by wiping. The cleaning products may be diluted with water prior to application as directed by instructions on product labels.

The finished cosmetic products containing the notified chemical at ≤ 0.1 % concentration will be used by consumers and professionals, such as beauticians and hairdressers. Depending on the nature of the cosmetic products, application of products may be done by hand, sprayed or through the use of an applicator.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

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

EXPOSURE DETAILS

Transport and storage workers
Transport, storage and warehouse workers may come into contact with the notified chemical or products containing the notified chemical, only in the event of accidental rupture of containers.

Reformulation workers
At the reformulation sites, dermal, ocular and inhalation exposure of workers to the notified chemical at various concentrations up to 100% may occur during handling of the notified chemical or mixtures containing the notified chemical, including weighing and transfer, blending, quality control analysis and cleaning/maintenance of equipment. The notifier stated that exposure is expected to be minimised through the use of engineering controls including mechanical ventilation and/or enclosed automated systems, and through the use of personal protective equipment (PPE) such as protective clothing, eye protection and impervious gloves.

Professional end users
Exposure to the notified chemical at ≤ 0.1 % concentration in end-use products may occur in professions where the services provided involve the application of cosmetic products to clients or the use of cleaning products in the cleaning industry. The principal route of exposure is expected to be dermal, while ocular and inhalation exposures are also possible. Professionals may use some PPE to minimise repeated or prolonged exposure and ensure that good hygiene practices are 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 the same 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 ≤ 0.1 % concentration through the use of the cosmetic and household products. The main route of exposure will be dermal, while ocular and inhalation exposures are also possible, particularly if the products are applied by spray.

Data on typical use patterns of various types of consumer products (SCCS, 2012; Cadby *et al.*, 2002; ACI, 2010; Loretz *et al.,* 2006) in which the notified chemical may be used are shown in the following tables. For the purposes of the exposure assessment, Australian use patterns for the various product categories are assumed to be similar to those in Europe. A dermal absorption (DA) of 100% was assumed for the notified chemical for calculation purposes. For the inhalation exposure assessment, a 2-zone approach was applied (Steiling *et al.*, 2014; Rothe *et al.*, 2011; Earnest, Jr, 2009). An adult inhalation rate of 20 m^3/day (enHealth, 2012) was used and it was conservatively assumed that the fraction of the notified chemical inhaled is 50%. For calculation purposes, a lifetime average female body weight (BW) of 64 kg (enHealth, 2012) was used.

Cosmetic products (Dermal exposure)

Product type	Amount (mg/day)	C (%)	RF (unitless)	Daily systemic exposure (mg/kg bw/day)
Body lotion	7,820	0.04	1	0.0489
Face cream	1,540	0.04	1	0.0096
Hand cream	2,160	0.04	1	0.0135
Deodorant	1,500	0.04	1	0.0094
Fine fragrances	750	0.1	1	0.0117
Hair styling products	4,000	0.04	0.1	0.0025
Shower gel	18,670	0.04	0.01	0.0012
Hand wash soap	20,000	0.04	0.01	0.0013
Shampoo	10,460	0.04	0.01	0.0007
Conditioner	3,920	0.04	0.01	0.0002
Total				**0.0990**

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

Household products (Indirect dermal exposure - from wearing clothes)

Product type	Amount (g/use)	C (%)	Product Retained (PR) (%)	Percent Transfer (PT) (%)	Daily systemic exposure (mg/kg bw/day)
Laundry liquid	230	0.1	0.95	10	0.0034
Fabric softener	90	0.1	0.95	10	0.0013
Total					**0.0048**

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

Household products (Direct dermal exposure)

Product type	Frequency (use/day)	C (%)	Contact Area (cm^2)	Product Use C (g/cm^3)	Film Thickness (cm)	Time Scale Factor	Daily systemic exposure (mg/kg bw/day)
Laundry liquid	1.43	0.1	1980	0.01	0.01	0.007	0.0000
Dishwashing liquid	3	0.1	1980	0.009	0.01	0.03	0.0003
All-purpose cleaner	1	0.1	1980	1	0.01	0.007	0.0022
Total							**0.0025**

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

Aerosol products (Inhalation exposure)

Product type	Amount	C	Inhalation Rate	Exposure Duration (Zone 1)	Exposure Duration (Zone2)	Fraction Inhaled	Volume (Zone 1)	Volume (Zone 2)	Daily systemic exposure
	(g/day)	(%)	(m^3/day)	(min)	(min)	(%)	(m^3)	(m^3)	(mg/kg bw/day)
Hair spray	9.89	0.04	20	1	20	50	1	10	**0.0013**

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

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above tables that contain the notified chemical. This would result in a combined internal dose of 0.1076 mg/kg bw/day. It is acknowledged that inhalation exposure to the notified chemical from use of other cosmetic and household products (in addition to hair spray) may occur. However, it is considered that the combination of the conservative (screening level) hair spray inhalation exposure assessment parameters, and the aggregate exposure from use of the dermally applied products, which assumes a conservative 100% absorption rate, is sufficiently protective to cover additional inhalation exposure to the notified chemical from use of other spray cosmetic and household products with lower exposure factors (e.g. air fresheners).

6.2. Human Health Effects Assessment

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

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2,000 mg/kg bw
Rabbit, skin irritation	irritating
Mouse, skin sensitisation – Local lymph node assay using the Integrated Model for the Differentiation of Skin Reactions (IMDS)	evidence of sensitisation
Human, skin sensitisation – RIPT (10%)	no evidence of sensitisation
Rat, combined repeated dose oral toxicity with reproduction and developmental toxicity screening test– 28 days.	NOAEL > 1,000 mg/bg bw/day for systemic and reproduction/developmental toxicity
Genotoxicity – *in vitro* mammalian cell micronucleus test	non mutagenic

Toxicokinetics, metabolism and distribution

No toxicokinetics, metabolism and distribution study data were submitted for the notified chemical.

Based on the molecular weight (< 500 g/mol) of the notified chemical, there is potential for the chemical to cross biological membranes. However, absorption is expected to be limited based on the relatively low water solubility (0.002 g/L at 20 °C) and the partition coefficient (log Pow ≥ 5.2) of the notified chemical.

Acute toxicity

The notified chemical has low acute oral toxicity in rats, with an LD50 > 2,000 mg/kg bw. Hunched posture and piloerection were observed in the animals shortly after application of the notified chemical at 2,000 mg/kg bw. The behaviour of the animals returned to normal within 6 hours. No further abnormalities were noted during the study.

No information was submitted for the notified chemical on acute dermal and acute inhalation toxicity.

Irritation and sensitisation

Based on a study conducted in rabbits, the notified chemical was considered to be irritating to the skin. Slight oedema was observed in all animals within 1 hour of the treatment. Slight to well-defined erythema was observed in all animals within 1 hour and progressed to moderate or severe erythema within 72 hours. All animals showed scaly formations after 7 days, which persisted to Day 14 and fully recovered within 21 days.

No information on eye irritation was provided for the notified chemical.

A local lymph node assay (LLNA), with a non-radioactive method conducted at 10%, 25% and 50% of the notified chemical in acetone/olive oil (4:1), gave lymph node cell count indexes of 1.09, 1.94 and 2.31 and ear thickness increase of 0.0013, 0.013 and 0.0213 mm when compared with the negative control. Differentiation

index (DI) was calculated and a value of > 1 was considered indicative of sensitisation potential (Vohr *et al*., 2000). Based on the assay results, the notified chemical was determined to have DI of 4.48 and 3.25 at 25% and 50% concentrations, respectively, and therefore considered by the study authors to be positive for skin sensitisation.

The notified chemical was tested in a human repeated insult patch test (HRIPT) at 10% concentration in diethylphthalate/ethanol (3:1) with 104 subjects in 2 separate panels completed the test. The notified chemical showed no visible skin reactions at this concentration for the full duration of the test.

Repeated dose toxicity and reproduction/developmental toxicity
A combined repeated dose oral toxicity study with the reproduction and developmental toxicity screening test was conducted on the notified chemical. Does levels tested were 100, 300 and 1,000 mg/kg bw/day taking peanut oil as the vehicle control and the notified chemical was given via oral gavage in male rats for at least 28 consecutive days and in female rats until Day 4 post-partum (approximately 49 consecutive days).

No treatment-related adverse parental, reproduction or developmental toxicity effects or toxicologically relevant changes were observed in any of the dose levels tested. A No Observed Adverse Effect Level (NOAEL) was established by the study authors for the notified chemical as > 1,000 mg/kg bw/day in rats for systemic toxicity and reproduction/developmental toxicity, based on the highest dose level tested.

Mutagenicity/Genotoxicity
An *in vitro* mammalian cell micronucleus test was carried out with the notified chemical. In both 4 hour and 20 hour exposure periods up to the cytotoxic and/or precipitating concentrations of the notified chemical, with or without metabolic activation, no relevant increases in the number of cells carrying micronuclei were observed. The micronucleus rate of cells treated with the notified chemical was within the range of historical control data. The results of the test were negative under the conditions of the test.

Health hazard classification
Based on the available information, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard classification	***Hazard statement***
Skin irritation (Category 2)	H315 – Causes skin irritation
Skin sensitisation (Category 1)	H317 – May cause an allergic skin reaction

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Reformulation
During reformulation, workers may be at risk of skin irritation and sensitisation when handling the notified chemical as introduced at various concentrations up to 100%. Data on eye irritation of the notified chemical were not provided. The notifier anticipates that worker exposure will be limited through the use of engineering controls such as enclosed systems, automated processes and local exhaust ventilation. The use of appropriate PPE (coveralls, imperious gloves and eye protection) will also be used to limit worker exposure.

End-Use
Workers involved in professional cleaning or the application of cosmetic products containing the notified chemical to clients (*e.g.* beauty salon workers) may be exposed to the notified chemical at ≤ 0.1% concentration. The principal route of exposure will be dermal, while ocular and inhalation exposure are also possible. PPE may be employed by workers to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, the risk to such workers is expected to be of a similar or lesser extent than that for consumers using the various products containing the notified chemical.

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

6.3.2. Public Health

Members of the public will experience widespread and frequent exposure to the notified chemical at ≤ 0.1% concentration through daily use of cosmetic and household cleaning products. The main route of exposure is expected to be dermal, while ocular and inhalation exposure are also possible, particularly if products are applied by spray.

Skin sensitisation

Proposed methods for the quantitative risk assessment (QRA) 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 0.1% concentration), as a worst case scenario, the Consumer Exposure Level (CEL) for the notified chemical is estimated to be 3.75 μg/cm^2/day (Cadby *et al.,* 2002). Based on available information, this CEL is unlikely to exceed the acceptable exposure level (AEL) derived from the LLNA study. Therefore, the risk to the public of induction of sensitisation that is associated with the use of fine fragrances containing the notified chemical is not considered to be unreasonable. Based on the lower expected exposure level from other cosmetic and household product types, by inference, the risk of induction of sensitisation associated with the use of these products containing the notified chemical 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 potential systemic exposure to the public from the use of the notified chemical in cosmetic and household products was estimated to be 0.1076 mg/kg bw/day (see Section 6.1.2). Using the NOAEL of 1,000 mg/kg bw/day derived from a combined repeated dose oral toxicity study with reproductive/developmental toxicity screening test, the margin of exposure (MOE) was estimated to be greater than 100, and is considered acceptable to account for intra- and inter-species differences.

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at ≤ 0.1% concentration in cosmetic and household products is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported into Australia as a component of end use cosmetic and household products; or imported in neat form or fragrance preparations for local reformulation into the end-use products. In general, the reformulation processes are expected to involve automated blending operation in an enclosed environment, followed by packing of the finished products into end-use containers. Wastewater from reformulation equipment cleaning containing the notified chemical is expected to be disposed of in accordance with local government regulations. Release of the notified chemical 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 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 import and 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 containers are rinsed before recycling through an approved waste management facility.

7.1.2. Environmental Fate

Following its use in cosmetic and household products, the majority of the notified chemical will enter the sewers and be treated at sewage treatment plants (STPs) before potential release to surface waters nationwide. A proportion of the notified chemical may be released to air. The half-life of the notified chemical in air is

calculated to be < 4 h, based on reactions with hydroxyl radicals (US EPA, 2012; calculated using AOPWIN v1.92). Therefore, the notified chemical is not expected to persist in the air compartment.

A ready biodegradation test conducted on the notified chemical indicates that it is readily biodegradable (65% degradation over 28 days). For details of the biodegradation study, refer to Appendix B. The notified chemical is expected to highly sorb to sludge at STPs based on its low water solubility (0.002 g/L) and high calculated partition coefficient (log P_{ow} = 5.2 – 6.2). Therefore, the notified chemical is expected to be removed effectively at STPs through biodegradation and adsorption to sludge, and only a small portion of the notified chemical may be released to surface waters. A proportion of the notified chemical may be applied to land when effluent is used for irrigation or when sewage sludge is used for soil remediation, or disposed of to landfill. The notified chemical residues in landfill and soils are expected to have low mobility based on its calculated soil adsorption coefficient (log K_{oc} = 2.5 – 4.1). The notified chemical is not expected to be bioaccumulative based on its ready biodegradability. 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 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 0.56 µg/L may potentially result in a soil concentration of approximately 3.74 µg/kg. Due to the notified chemical's ready biodegradability, annual accumulation is not expected.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on an acceptable analogue of the notified chemical are summarised in the table below. Details of the study can be found in Appendix B.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h LC50 = 1.82 mg/L	Toxic to fish

The above ecotoxicological endpoint for the acceptable analogue indicates that the notified chemical is toxic to aquatic organisms. However, as only one ecotoxicological endpoint was provided, the notified chemical was not formally classified under the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS) (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

The predicted no-effects concentration (PNEC) has been calculated based on the endpoint for fish as shown in the table below. A conservative safety factor of 1,000 was used given the acute endpoint for only one trophic level is available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC 50 for fish	1.82	mg/L
Assessment Factor	1,000	
Mitigation Factor	1.00	
PNEC:	1.82	µg/L

7.3. Environmental Risk Assessment

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

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.56	1.82	**0.31**
Q - Ocean	0.06	1.82	**0.03**

The conservative risk quotients (Q = PEC/PNEC) for the worst-case discharge scenario have been calculated to be less than 1 for both riverine and ocean compartments indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations based on its annual importation quantity and use pattern. Therefore, based on the calculated risk quotients, the notified chemical is not considered to pose an unreasonable risk to the environment.

APPENDIX A: TOXICOLOGICAL INVESTIGATIONS

A.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method EC Council Regulation No 440/2008 B.1 tris Acute Oral Toxicity – Acute Toxic Class Method
Species/Strain	Rat/Wistar Crl:WI
Vehicle	Sunflower oil
Remarks - Method	GLP compliance statement No significant protocol deviations

RESULTS

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

LD50	> 2,000 mg/kg bw
Signs of Toxicity	Hunched posture and piloerection was seen in the animals after application of the test substance. The behaviour of all animals returned to normal within 6 hours.
Effects in Organs	No pathological abnormalities were observed in any animal.
Remarks - Results	The animals showed expected body weight gain over the observation period.

CONCLUSION	The notified chemical is of low acute toxicity via the oral route.
TEST FACILITY	Frey-Tox (2006a)

A.2. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion EC Directive 2004/73/EC B.4 Acute Toxicity (Skin Irritation)
Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	None. The notified chemical was directly applied.
Observation Period	21 days
Type of Dressing	Semi-occlusive
Remarks - Method	GLP compliance statement No significant protocol deviations

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	1.67	2.67	2.67	3	< 21 days	0
Oedema	0.33	1.33	1.33	2	< 21 days	0

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

Remarks - Results	Slight oedema was observed in all animals within 1 hour of applying the notified chemical. Slight to well-defined erythema was observed in all animals within 1 hour, which became severe within 72 hours. All animals showed scaly formations after 7 days, which fully recovered within 21

days.

CONCLUSION The notified chemical is irritating to the skin.

TEST FACILITY Frey-Tox (2006b)

A.3. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE Notified chemical

METHOD OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
EC Directive 2004/73/EC B.42 Skin Sensitisation (Local Lymph Node Assay)

Species/Strain	Mouse/Crl:NMRI
Vehicle	Acetone/olive oil (4:1)
Preliminary study	No
Positive control	Not conducted in parallel with the test substance, but had been conducted previously in the test laboratory using α-hexylcinnamaldehyde.
Remarks - Method	GLP compliance statement LLNA method using the Integrated Model for Differentiation of Skin Reactions (IMDS)

RESULTS

Test Substance Concentration (% w/w)	*Number and Sex of Animals*	*Lymph Node Cell Count Index*	*Ear Thickness Increase (mm)*
0 (vehicle control)	6F	1.00	0
10	6F	1.09	0.0013
25	6F	1.94	0.013
50	6F	2.31	0.0213

Test Substance Concentration (% w/w)	*% of Lymph Node Cell Count Index to the Max.**	*% of Ear Thickness Increase to the Max.**	*Differential Index (DI)**
10			
25	38.80	8.67	4.48
50	46.20	14.20	3.25

* The LLNA-IMDS model defines a maximum ear thickness increase of 0.15 mm and a maximum lymph node cell count index of 5 (Vohr *et al*., 2000). The defined maximum values were set as 100%, and the lymph node cell count index and ear thickness increase were converted as percentages of the defined maximums respectively. Differentiation index (DI) was calculated by dividing the percentage of lymph node cell count index to the maximum with the percentage of ear thickness increase to the maximum.

Remarks - Results DI was calculated to distinguish between inflammatory (non-specific) and allergic (specific) reactions. This was used to quantify the activation of the local draining lymph nodes. DI > 1 was considered to indicate an allergic skin reaction.

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

TEST FACILITY Frey-Tox (2006c)

A.4. Skin sensitisation – human volunteers

TEST SUBSTANCE Notified chemical (10% in vehicle)

METHOD Repeated insult patch test with challenge

Study Design Induction Procedure: Patches containing 0.2 mL test substance were applied 3 times per week (Monday, Wednesday and Friday) for a total of 9

applications. Patches were removed by the participants after 24 h and graded after an additional 24 h (or 48 h if the participant was unable to report on time).

Rest Period: 24 – 48 hours

Challenge Procedure: 2 weeks after the final induction application, a patch was applied to a naïve site. Patches were removed by the participants after 24 h. Sites were graded 24 and 72 h post-patch removal.

Study Group	89 F, 15 M; age range 17 – 78 years
Vehicle	Diethyl phthalate/ethanol (3:1)
Remarks - Method	Occluded. The test substance was spread on a 3/4 × 3/4 in^2 (approximately 2 × 2 cm^2) patch.

RESULTS

Remarks - Results	In this study, 115 qualified test subjects were selected into 2 panels in which 104 subjects completed and 11 subjects discontinued for reasons unrelated to the study.
	No visible skin reactions were observed for any test subject throughout the entire test.
CONCLUSION	The notified chemical at 10% concentration was non-sensitising under the conditions of the test.
TEST FACILITY	CPT (2006)

A.5. Repeat dose toxicity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 422 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test
Species/Strain	Rat/Wistar Crl:WI (Han)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: ≥ 28 days (males), ~49 days (females) Dose regimen: 7 days per week Post-exposure observation period: None
Vehicle	Peanut oil
Remarks - Method	GLP compliance statement
	No significant protocol deviations
	The test substance was administered to male rats for at least 28 days and to female rats for 14 days prior to pairing, through the pairing and gestation periods until the F1 generation reached day 4 post-partum.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
control	20 (10F, 10M)	0	0/20
low dose	20 (10F, 10M)	100	0/20
mid dose	20 (10F, 10M)	300	0/20
high dose	20 (10F, 10M)	1,000	0/20

Mortality and Time to Death

There were no unscheduled deaths of treated animals in all dose groups.

Clinical Observations

No treatment-related clinical signs were observed in treated animals in all dose groups.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

No treatment-related effects on haematology or clinical biochemistry parameters were observed in treated animals in all dose groups.

Effects in Organs

A statistically significant increase of liver weights was noted in males and females of the high dose group. An increased incidence of centrilobular to diffuse hepatocellular hypertrophy were observed in males of the mid dose group, and both males and females in the high dose group.

In the absence of any liver injury, the changes in the liver were considered by the study authors to be a metabolic adaptation and not an adverse effect.

Effects on Parental (P) animals:

Systemic Toxicity

No treatment-related adverse effects were observed in treated animals in all dose groups.

Reproductive Toxicity

No effects on mating performance, fertility, corpora lutea count, duration of gestation, implantation rate, post-implantation loss, litter size and post-natal loss were observed for all parental animals at any dose level.

Effects on 1st Filial Generation (F1)

No treatment-related adverse effects were observed in pups and pups sex ratio was not affected.

Remarks – Results

The study authors stated that there were no toxicologically relevant adverse effects observed in animals treated up to 1,000 mg/kg bw/day.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established as > 1,000 mg/kg bw/day by the study authors for systemic toxicity and reproduction/development toxicity.

TEST FACILITY Harlan (2012)

A.6. Genotoxicity – *in vitro* mammalian cell micronucleus test

TEST SUBSTANCE Notified chemical

METHOD OECD TG 487 *In vitro* Mammalian Cell Micronucleus Test

Species/Strain	Human peripheral blood cells
Cell Type/Cell Line	Lymphocytes
Metabolic Activation System	S9-Mix from phenobarbital (PB)/β-naphthoflavone (NF) induced rat liver
Vehicle	DMSO
Remarks - Method	GLP Certificate

As dose range-finding studies, 2 preliminary cytotoxicity tests were carried out at 0.02 – 5 µL/mL and 0.0001 – 5 µL/mL. The dose selection for the main experiments was based on cytotoxicity observed in the range-finding study and solubility test.

Vehicle and three positive controls (demecolcin, mitomycin C and cyclophosphamide) were run concurrently with the notified chemical.

Metabolic Activation	*Test Substance Concentration (µL/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0.0039, 0.0078*, 0.0156*, 0.0313*, 0.0625, 0.125, 0.25, 0.5, 1.0, 1.5, 2.0, 2.5, 5.0	4 h	40 h

Metabolic Activation	*Test Substance Concentration (µL/mL)*	*Exposure Period*	*Harvest Time*
Test 2	0.00049, 0.00098, 0.00195, 0.0039, 0.0078, 0.0156*, 0.0313*, 0.0625*, 0.125, 0.25, 0.5, 1.0, 2.0	20 h	40 h
Present			
Test 1	0.00012, 0.00024, 0.00049*, 0.00098*, 0.00195, 0.0039, 0.0078, 0.0156, 0.0313, 0.0625, 0.125, 0.25, 0.5, 1.0*, 2.0, 3.0, 4.0, 5.0	4 h	40 h
Test 2	0.00012, 0.00024, 0.00049, 0.00098, 0.00195*, 0.0039*, 0.25*, 0.5*, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 5.0	4 h	40 h

*Cultures selected for micronucleus analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µL/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation in Main Test*	*Genotoxic Effect*
Absent				
Test 1	> 5	≥ 0.25	≥ 0.0313	Negative
Test 2	≥ 0.099	≥ 0.0625	≥ 0.25	Negative
Present				
Test 1	> 5	≥ 3.0	≥ 0.00098	Negative
Test 2	≥ 5	≥ 0.5	≥ 0.0039	Negative

Remarks - Results

The notified chemical did not cause any increase in the number of cells carrying micronuclei in either the absence or presence of metabolic activation when tested up to cytotoxic and/or precipitating concentrations. The micronucleus rate of the treated cells was within the range of historical control data.

The positive and vehicle controls gave satisfactory responses confirming the validity of the test system.

CONCLUSION

The notified chemical was not genotoxic to human lymphocytes treated *in vitro* under the conditions of the test.

TEST FACILITY

Harlan CCR (2011)

APPENDIX B: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

B.1. Environmental Fate

B.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test
Inoculum	Activated sludge from a municipal STP
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	CO_2 was analysed by Shimadzu TOC 5000A Analyser
Remarks - Method	No significant deviations from the test guidelines were reported. The test substance was injected into sealed test bottles containing the inoculated mineral medium using a micro syringe. A toxicity control was run.

RESULTS

Test substance		*1-octanol*	
Day	*% Degradation*	*Day*	*% Degradation*
2	19.3	2	31.6
7	57.3	7	76.9
14	63.7	14	80.6
21	65.4	28	81.2

Remarks - Results	All validity criteria for the test were satisfied. The percentage degradation of the reference compound, 1-octanol surpassed the threshold level of 60% within 14 days indicating the suitability of the inoculums. The toxicity control exceeded 25% biodegradation after 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The degree of degradation of the test substance after 28 days was 65% and the 10 day window was passed.
CONCLUSION	The test substance is readily biodegradable.
TEST FACILITY	Harlan (2011)

B.2. Ecotoxicological Investigations

B.2.1. Acute toxicity to fish

TEST SUBSTANCE	Analogue chemical (2-Methyl decanal)
METHOD	OECD TG 203 Fish, Acute Toxicity Test – Semi Static EC Council Regulation No 440/2008 C.1 Acute Toxicity for Fish - Semi Static
Species	Ricefish – (*Oryzias latipes*)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	Not provided
Analytical Monitoring	Gas Chromatography
Remarks – Method	No significant deviations from the test guidelines were reported. A test solution with a loading rate of 100 mg/L was prepared, sonicated for 15 minutes and stirred for 3 hours, then filtered (0.7 µm). This saturated solution was diluted to achieve lower test concentrations. The test media was renewed daily. The test concentrations were measured from freshly prepared media at 0, 24, 48, 72 hours and from the corresponding 24 hour old media.

RESULTS

Concentration (mg/L)		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	Control	10	0	0	0	0	0
2.03	0.21	10	0	0	0	0	0
4.43	0.43	10	0	0	0	0	0
9.65	0.97	10	0	0	5	6	6
21.0	2.15	10	2	10	10	10	10
45.9	10.08 (saturated solution)	10	10	10	10	10	10

LC50	= 1.819 mg/L (95% CL: 1.304 – 2.564 mg/L) at 96 hours (calculated by Probit method and Moving Average Angle method)
Remarks – Results	All validity criteria for the test were satisfied. The dissolved oxygen concentration in the test solution during the test was ≥ 61%. The concentrations of aged test media were within ±20% of fresh media. Nevertheless, all test results were calculated based on the arithmetic mean measured concentrations.

CONCLUSION The test substance is toxic to fish.

TEST FACILITY Biotoxtech (2014)

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