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January 2020

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Oils, Aquilaria crassna

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	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/2095	International Flavours and Fragrances (Australia) Pty Ltd	Oils, Aquilaria crassna	Yes	≤ 1 tonne per annum	Fragrance ingredient

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Hazard classification	*Hazard statement*
Skin corrosion (Category 1)	H314 – Causes severe skin burns and eye damage

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 2)	H411 – Toxic to aquatic life with long lasting effects

Human Health Risk Assessment
Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

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 corrosion (Category 1): H314 – Causes severe skin burns and eye damage

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

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
  - Local exhaust ventilation

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

- 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:
  - Impervious gloves
  - Safety glasses or goggles
  - Protective clothing
  - Respiratory protection if aerosols or mists are expected to be generated

  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.

Emergency procedures

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

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.

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 0.1% in cosmetic and household products;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a fragrance ingredient, 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
International Flavours and Fragrances (Australia) Pty Ltd (ABN: 77 004 269 658)
310 Frankston-Dandenong Road
DANDENONG VIC 3175

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)
Schedule data requirements are varied for all physical and chemical properties, except for vapour pressure and flash point.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT
None

NOTIFICATION IN OTHER COUNTRIES
Canada, USA

2. IDENTITY OF CHEMICAL

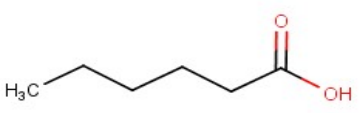
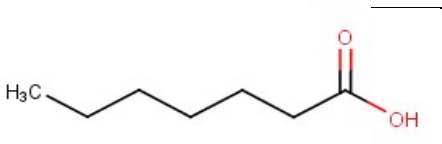
MARKETING NAME
Oud oil

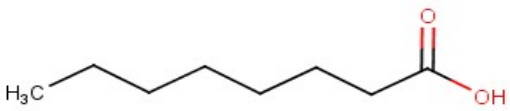
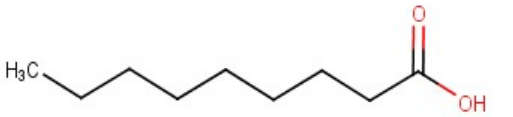
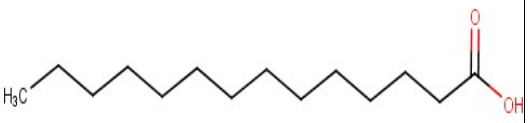
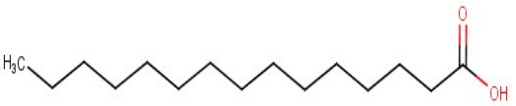
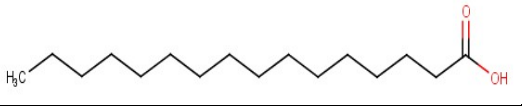
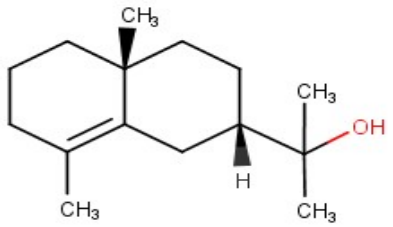
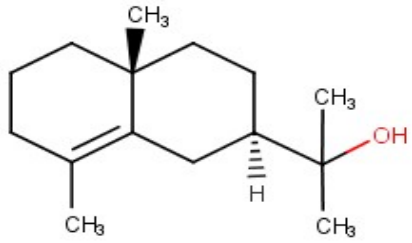
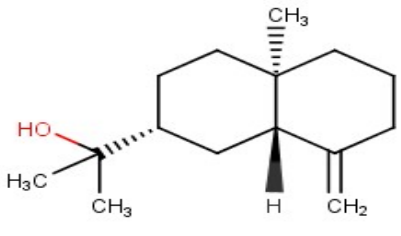
CAS NUMBER
958663-49-5

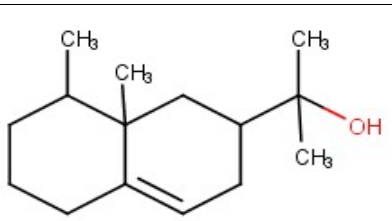
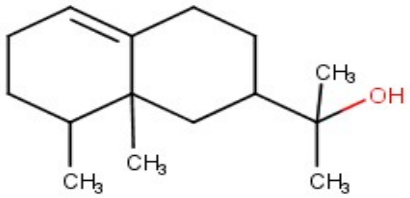
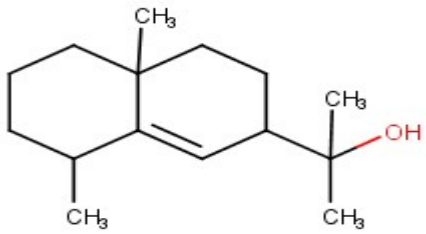
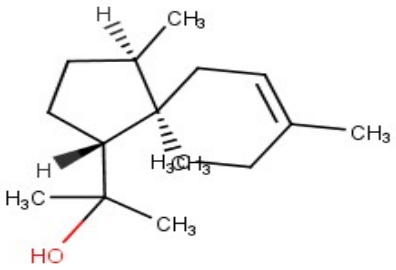
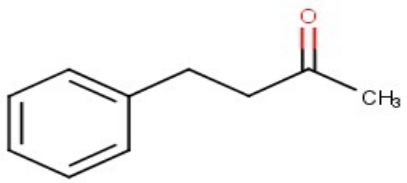
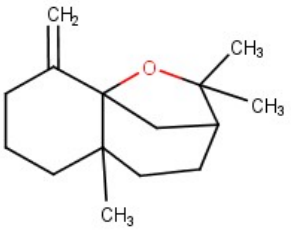
CHEMICAL NAME
Oils, Aquilaria crassna

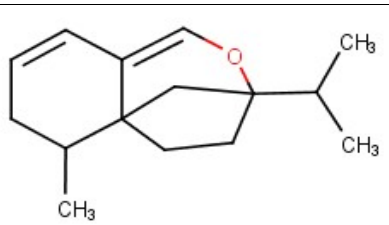
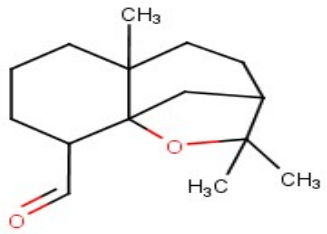
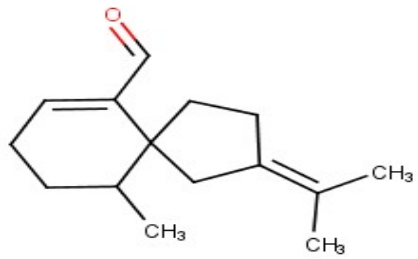
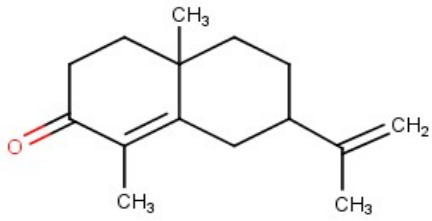
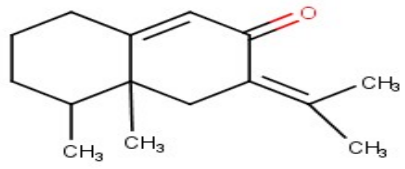
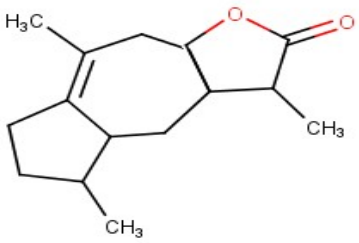
OTHER NAME
Agarwood oil

MOLECULAR FORMULA, STRUCTURAL FORMULA AND MOLECULAR WEIGHT
The notified chemical is an UVCB substance comprising a complex mixture of constituents (see table below). The notifier has identified 60.7% of the constituents by GC-MS, including a range of aliphatic acids (27.38%) and terpineol type substances (22.63%). The unknowns, comprising 39.7% of the UVCB substance, consist of 165 constituents (one at 3.15% and 164 at < 1%). The molecular weight range of the known constituents is 116-256 g/mol.

Name	CAS Number	Molecular formula	Structural formula	Molecular weight (g/mol)	Percentage
Aliphatic acids					
Hexanoic acid	142-62-1	$C_6H_{12}O_2$		116	1.44
Hepatonic acid	111-14-8	$C_7H_{14}O_2$		130	3.47

Name	CAS Number	Molecular formula	Structural formula	Molecular weight (g/mol)	Percentage
Octanoic acid	124-07-2	$C_8H_{16}O_2$		144	10.89
Nonanoic acid	112-05-0	$C_9H_{18}O_2$		158	2.16
Tetradecanoic acid	544-63-8	$C_{14}H_{28}O_2$		228	1.29
Pentadecanoic acid	1002-84-2	$C_{15}H_{30}O_2$		242	1.51
Hexadecanoic acid	57-10-3	$C_{16}H_{32}O_2$		256	6.62
Total					**27.38**
Terphenol type substances					
2-Naphthalenemethanol, 1,2,3,4,4a,5,6,7-octahydro-α,α,4a,8-tetramethyl-, (2*S*,4a*R*)-*rel*-	13902-07-3	$C_{15}H_{26}O$		222	2.21
2-Naphthalenemethanol, 1,2,3,4,4a,5,6,7-octahydro-α,α,4a,8-tetramethyl-, (2*R*,4a*R*)-*rel*-	13902-07-3	$C_{15}H_{26}O$		222	2.29
2-Naphthalenemethanol, decahydro-α,α,4a-trimethyl-8-methylene-	92790-78-8	$C_{15}H_{26}O$		222	2.08

Name	CAS Number	Molecular formula	Structural formula	Molecular weight (g/mol)	Percentage
2-Naphthalenemethanol, 1,2,3,5,6,7,8,8a-octahydro-α,α,8,8a-tetramethyl-, (2*R*,8*R*,8a*S*)-*rel*-	43206-16-2	$C_{15}H_{26}O$		222	3.53
2-Naphthalenemethanol, 1,2,3,5,6,7,8,8a-octahydro-α,α,8,8a-tetramethyl-, (2*R*,8*R*,8a*S*)-*rel*-	43206-16-2	$C_{15}H_{26}O$		222	5.28
2-Naphthalenemethanol, 2,3,4,4a,5,6,7,8-octahydro-α,α,4a,8-tetramethyl-	872796-38-8	$C_{15}H_{26}O$		222	1.02
Rel-2-[(1*R*,4*R*,5*R*)-4,8-dimethylspiro[4,5]dec-7-en-1-yl]propan-2-ol	unassigned			222	6.22
Total					**22.63**
2-Butanone, 4-phenyl-	2550-26-7	$C_{10}H_{12}O$		148	1.57
Total					**1.57**
2,2,5a-trimethyl-9-methyleneoctahydro-2*H*-3,9a-methanobenzo[b]oxepine	unassigned			220	1.93

Name	CAS Number	Molecular formula	Structural formula	Molecular weight (g/mol)	Percentage
3*H*-3,5a-Methano-2-benzoxepin, 4,5,6,7-tetrahydro-6-methyl-3-(1-methylethyl)-, (3α,5aβ,6β)	168099-24-9	$C_{15}H_{22}O$		218	1.16
2,2,5a-Trimethyloctahydro-2*H*-3,9a-methanobenzo[b]oxepine-9-carbaldehyde	unassigned			236	1.27
Spiro[4.5]dec-6-ene-6-carboxaldehyde, 10-methyl-2-(1-methylethylidene)-,*cis*-	168099-21-6	$C_{15}H_{22}O$		218	1.31
2(3*H*)-Naphthalenone, 4,4a,5,6,7,8-hexahydro-1,4a-dimethyl-7-(1-methylethenyl)-	60026-22-4	$C_{15}H_{22}O$		218	1.05
4a,5-Dimethyl-3-(propan-2-ylidene)-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one	unassigned			218	1.47
3,5,8-Trimethyl-3a,4,4a,5,6,7,9,9a-octahydroazuleno[6,5-b]furan-2(3*H*)-one	unassigned			234	0.93
Total					**9.12**
Unknown	n/a	n/a	n/a	220	3.15
Unknown	n/a	n/a	n/a	-	36.15 (164 peaks at < 1%)

ANALYTICAL DATA

Reference IR, GC-MS, UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
100% (UVCB)

HAZARDOUS IMPURITIES
None

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% BY WEIGHT)
None
ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Liquid

Property	*Value*	*Data Source/Justification*
Melting Point	12.8-116.4 °C	Estimated for known constituents (US EPA, 2012)
Boiling Point	208-359 °C	Estimated for known constituents (US EPA, 2012)
Density	934-984 kg/m^3	SDS
Vapour Pressure	1.92 x 10^{-3} kPa at 24 °C	Measured
Water Solubility	4.0 x 10^{-5} - 5.898 g/L	Estimated using QSAR
Hydrolysis as a Function of pH	Not determined	The majority of the UVCB constituents are hydrolytically stable. However, a small percentage of the constituents have functionalities which are susceptible to hydrolysis but this is not expected to be significant in the environmental pH range (4-9)
Partition Coefficient (n-octanol/water)	log Pow = 2.05 – 6.96 log Pow = 3.12 – 5.55 Log Pow = 1.96 – 5.49	Aliphatic acid constituents (27.38%) Terpeneol constituents (22.63%) Aliphatic spiro and cyclic lactone constituents (9.12%) Estimated by KOWWIN v.1.68 (US EPA, 2012)
Adsorption/Desorption	log K_{oc} = 1.22 – 4.12 log K_{oc} = 3.08 – 3.25 Log K_{oc} = 2.23 – 3.89	Aliphatic acid constituents (27.38%) Terpeneol constituents (22.63%) Aliphatic spiro and cyclic lactone constituents (9.12%) Estimated by KOCWIN v.2.00 (US EPA, 2012)
Dissociation Constant	Not determined	Contains several anionic functionalities which are expected to be ionised in the environmental pH range (4 - 9)
Flash Point	104 °C at 101.3 kPa	Measured
Flammability	Not determined	Combustible liquid
Autoignition Temperature	Not determined	Estimated > 104 °C based on measured flash point
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties

DISCUSSION OF PROPERTIES
For details of tests on physical and chemical properties, refer to Appendix A.

Reactivity
The notified chemical is expected to be stable under normal conditions of use.

Physical Hazard Classification
Based on the limited 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 104 ºC which is greater than 93 °C. Based on *Australian Standard AS1940* definitions for combustible liquid, the notified chemical may be considered as a Class C2 combustible liquid if the chemical has a flash point below the boiling point.

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 into Australia as a component of fragrance oil formulations at ≤ 10% concentration.

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

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

PORT OF ENTRY
Melbourne

IDENTITY OF RECIPIENTS
International Flavours and Fragrances (Australia) Pty Ltd

TRANSPORTATION AND PACKAGING
The notified chemical will be imported as a component of fragrance oil formulations in 208 L polypropylene-lined steel drums. Within Australia the drums will be transported mainly by road to the warehouse for storage and later distributed by road to formulators for reformulation. Finished consumer products containing the notified chemical will be transported primarily by road to retail stores in packages suitable for retail sale.

USE
The notified chemical will be used as a fragrance ingredient in cosmetic and household products at up to 0.1% concentration.

OPERATION DESCRIPTION
Reformulation of fragrance oil formulations containing the notified chemical at up to 10% concentration into finished consumer goods may vary depending on the type of product and may involve both automated and manual transfer steps. Typically, reformulation processes may incorporate blending operations that are highly automated and occur in a fully enclosed/contained environment, followed by automated filling of the reformulated end-use products into containers of various sizes.

End-use products containing the notified chemical at up to 0.1% concentration will be used by consumers and professionals such as hairdressers, beauticians or cleaners. Depending on the nature of the product, these could be applied in a number of ways, such as by hand, using an applicator or sprayed.

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	None	Incidental
Mixer and compounding	4	250
Drum handling	1	250
Drum cleaning	2	250
Equipment cleaning	2	250
Quality control	1	250
Professional users - hairdressers, cleaners etc.	8	250

EXPOSURE DETAILS

Transport and storage

Transport, storage and warehouse workers may come into contact with the notified chemical as a component of fragrance oil formulations at ≤ 10% concentration, only in the unlikely event of accidental rupture of containers.

Reformulation

During reformulation, dermal and ocular exposure of workers to the notified chemical at ≤ 10% concentration may occur during weighing and transfer stages, blending, quality control analysis, and cleaning and maintenance of equipment. Due to the low vapour pressure of the notified chemical (1.92×10^{-3} kPa at 24 °C), inhalation exposure is not expected, unless aerosols or mists are formed.

The notifier states that exposure is expected to be minimised through the use of local exhaust ventilation and/or enclosed systems, and through workers using personal protective equipment (PPE) such as protective clothing, goggles, impervious gloves and respiratory protection (in cases where there is inadequate ventilation).

End-use

Exposure to the notified chemical in end-use products at up to 0.1% concentration may occur in professions where the services provided involve the application of cosmetics to clients (e.g. hair dressers and workers in beauty salons), or the use of household products in the cleaning industry. The principal route of exposure will be dermal, while ocular and inhalation exposure are also possible. Such professionals may use some PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using the 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 up to 0.1% concentration through the use of a wide range of cosmetic and household products. The main route of exposure will be dermal, while ocular and inhalation exposure are also possible, particularly if products are applied by spray.

6.2. Human Health Effects Assessment

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

Endpoint	***Result and Assessment Conclusion***
Acute oral toxicity – rat	LD50 > 2,000 mg/kg bw; low toxicity
Skin sensitisation – mouse local lymph node assay	no evidence of sensitisation up to 50%
Skin sensitisation – HRIPT (n=103)	no evidence of sensitisation (at 16% induction concentration)
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* chromosome aberration test in human lymphocytes	non clastogenic

Toxicokinetics

Given the low molecular weight of the notified chemical (molecular weight range for known constituents: 116-256 g/mol), absorption across biological membranes may occur.

Acute Toxicity

The notified chemical is of low acute oral toxicity based on a study conducted in rats.

No acute dermal or inhalation toxicity studies of the notified chemical were provided.

Irritation

No skin or eye irritation studies of the notified chemical were provided.

The notified chemical contains constituents classified for skin corrosion. Hepatonic acid present at 3.47% is classified as a skin corrosive Category 1B and octanoic acid present at 10.89% is classified as a skin corrosive Category 1C (HCIS, Safe Work Australia). Based on the concentration of these two constituents, the notified chemical warrants classification for skin corrosion (Category 1) according to the GHS criteria.

Sensitisation
The notified chemical up to 50% concentration was not found to be a skin sensitiser in a mouse Local Lymph Node Assay (LLNA) with stimulation indices of 2.21, 2.32 and 2.87 at 0.5, 5 and 50% concentration, respectively.

In a human repeated insult patch test (HRIPT), the notified chemical at 16% induction concentrations in ethanol:diethyl phthalate (1:3) did not elicit a positive sensitisation response.

Repeated Dose Toxicity
No repeated dose toxicity study of the notified chemical was provided.

Mutagenicity/Genotoxicity
The notified chemical tested negative in a bacterial reverse mutation test and in an *in vitro* chromosome aberration test in human lymphocytes.

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

Hazard classification	***Hazard statement***
Skin corrosion (Categories 1)	H314 – Causes severe skin burns and eye damage

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
The notified chemical is considered corrosive. Based on its low molecular weight, the notified chemical may be absorbed across biological membranes; however, the systemic toxicity of the notified chemical is unknown.

Reformulation
Workers may experience dermal, ocular and perhaps inhalation exposure to the notified chemical at ≤ 10% concentration during reformulation. The use of local ventilation, enclosed/automated processes and PPE (i.e. protective clothing, goggles, impervious gloves and respiratory protection, if inhalation exposure may occur) are expected to be minimise the potential for exposure.

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

End-use
Cleaners and beauty care professionals will handle the notified chemical at up to 0.1% concentration, similar to public use. Such professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. Therefore, the risk to workers who use products containing the notified chemical is expected to be of a similar or lesser extent than consumers who use such products on a regular basis. For details of the public health risk assessment see section 6.3.2 below.

6.3.2. Public Health
Members of the public may experience repeated exposure to the notified chemical through the use of cosmetic and household products containing the notified chemical at up to 0.1% concentration.

Irritation
The notified chemical is considered corrosive, but significant irritation effects are not expected from the use of products containing the notified chemical at the proposed low use concentration (up to 0.1%) in cosmetic and household products.

Systemic toxicity
The repeated dose toxicity effects of the notified chemical have not been determined. However, exposure is expected to be limited by the low concentration of the notified chemical (up to 0.1%) in end use products.

Therefore, based on the information available, the risk to the public associated with use of the notified chemical at up to 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 fragrance oil formulations for local reformulation into finished cosmetic and household products. In general, the reformulation processes are expected to involve automated blending operations 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 to sewer via on-site wastewater treatment 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
The notified chemical is an UVCB substance comprising a complex mixture of 187 constituents, including aliphatic short and long chain carboxylic acids (7), terpeneols (8), aliphatic spiro and cyclic lactone compounds with side chain (7) and unidentified components (165). QSARs are suitable for discrete organic molecules and cannot be directly used to estimate the properties of UVCBs (EPHC, 2009). However, for well characterised complex (C) substances the properties of the UVCB may be estimated from consideration of the individual discrete organic molecules (ECHA, 2012). The majority of the constituents of the notified chemical have been identified and is comprised of aliphatic carboxylic acids, terpeneols and aliphatic spiro and cyclic lactone compounds (60.7%), and is therefore considered well characterised. However, 39.7% of the notified chemical is unidentified.

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 volatilise to air. The half-life of a major component of the notified chemical (hexadecanoic acid) in air is calculated to be 6.5 h, and the major component likely to be volatile from water based on low water solubility and chemical structure {*Rel*-2-[(1*R*,4*R*,5*R*)-4,8-dimethylspiro[4,5]dec-7-en-1-yl]propan-2-ol} is 1.2 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 not expected to be readily biodegradable (32.9% degradation over 28 days). For details of the biodegradation study, refer to Appendix C. The majority of the identified constituents of the notified chemical (60.7%) are expected to highly sorb to sludge at STPs based on their low water solubility and moderate to high estimated partition coefficient (log Pow 1.96 - 6.96). 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 majority of the identified components of the

notified chemical (60.7%) as residues in landfill and soils are expected to have low mobility based on their estimated soil adsorption coefficients (log K_{oc} = 1.22 - 4.12).

The majority of the identified components of the notified chemical (60.7%) are expected to bioaccumulate based on their moderate to high octanol-water partition coefficient value (log Pow = 1.96 - 6.96) and lack of ready biodegradability. However, the notified chemical is not expected to be significantly released to surface waters. 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	200.0	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	0%	**Mitigation**
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 0.377 µg/L may potentially result in a soil concentration of approximately 2.51 µg/kg. Due to the notified chemical's biodegradability, annual accumulation is not expected.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemical is summarised in the table below. Details of the study can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h LC50 = 5.06 mg/L	Toxic to fish

Based on the above ecotoxicological endpoint for the notified chemical, it is expected to be toxic to fish. Therefore, under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009), the notified chemical is formally classified as "Acute Category 2: Toxic to aquatic life". On the basis of acute toxicity and lack of biodegradability criteria, the notified chemical is formally classified as 'Chronic Category 2: Toxic to aquatic life with long-lasting effects".

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 1000 was used given the acute endpoint for only one trophic level is available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LC50 for fish	5.06	mg/L
Assessment Factor	1,000	
Mitigation Factor	1.00	

PNEC:	5.06 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	5.06	**0.11**
Q - Ocean	0.06	5.06	**0.01**

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 which 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 quotient, the notified chemical is not considered to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Vapour Pressure 1.92×10^{-3} kPa at 24 °C

Method	Equivalent to OECD TG 104 Vapour Pressure
Remarks	Determined using dynamic head space method
Test Facility	IFF (2018)

Flash Point 104 °C at 101.3 kPa

Method	EEC Directive 92/69 A.9 Flash Point
Remarks	Closed cup method
Test Facility	IFF (2018)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute Oral Toxicity – Rat

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 420 Acute Oral Toxicity – Fixed Dose Method
Species/Strain	Rat/Wistar (RccHan™:WIST)
Vehicle	Arachis oil BP
Remarks – Method	No protocol deviations. For the 2,000 mg/kg dose level, the test substance was used as supplied.

RESULTS

Sighting Study

Dose (mg/kg bw)	*Administered*	*Evident Toxicity*	*Mortality*
300	1 F	Nil	0/1
2,000	1 F	Nil	0/1

Signs of Toxicity	No signs of toxicity were noted.
Effects in Organs	No abnormalities were observed during necropsy.

Main Study

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	1 F	2,000	0/1
2	4 F	2,000	0/4

Discriminating Dose	> 2000 mg/kg bw
Signs of Toxicity	No signs of toxicity were observed.
Effects in Organs	No abnormalities were observed at necroscopy
Remarks – Results	All animals showed expected body weight gains during the study period.

CONCLUSION	The notified chemical is of low acute toxicity via the oral route.
TEST FACILITY	Harlan (2012a)

B.2. Skin Sensitisation – LLNA

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
Species/Strain	Mouse/CBA/Ca
Vehicle	Acetone/olive oil (4:1)
Preliminary study	Yes
Positive control	Not conducted in parallel with the test substance, but had been conducted previously in the test laboratory using α-hexylcinnamaldehyde (85%).
Remarks – Method	A preliminary test was conducted using 50%, 75% and 100% test substance to justify the dose concentrations for the main study. Very slight erythema was noted in all animals. The animals treated with 100% test substance showed > 25% increase in mean ear thickness. No excessive irritation indicated by a ≥ 25% increase in mean ear thickness was noted with 50% and 75% test substance. However, the 75% concentration was not considered suitable for the main test by the study authors given the marked increased in mean ear thickness (~18%).

RESULTS

Concentration (% w/w)	*Number and Sex of Animals*	*Proliferative Response (DPM/lymph node)*	*Stimulation Index (test/control ratio)*
Test Substance			
0 (vehicle control)	5 F	2317.0	-
0.5	5 F	5116.92	2.21
5	5 F	5375.7	2.32
50	5 F	6640.3	2.87
*Positive Control**			
25	5 F	-	5.76

* α-Hexylcinnamaldehyde (85%)

Remarks – Results

No unscheduled mortalities or signs of systemic toxicity were observed during the study period.

The stimulation index was < 3 in all test groups, indicating a non-sensitising response.

Very slight erythema was noted in animals treated with 50% test substance. No excessive irritation indicated by a ≥ 25% increase in mean ear thickness was noted at any dose concentration tested.

CONCLUSION

There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical up to 50% concentration.

TEST FACILITY

Harlan (2012b)

B.3. Skin Sensitisation – Human volunteers

TEST SUBSTANCE

Notified chemical (16% concentration)

METHOD

Study Design

Induction procedure: patches containing 0.15 mL of the test substance (16% of the notified chemical) were applied 3 times per week (Monday, Wednesday and Friday) for a total of 9 applications during the induction period. Patches were removed by the subjects after 24 hours and graded by technicians after an additional 24 hours (or 48 hours for patches applied on Friday).
Rest Period: ~10-21 days
Challenge Procedure: Patches containing the notified chemical at 16% concentrations were applied to a naïve site and were removed by technicians 24 hours after application. The sites were scored 24, 48 and 72 hours after application. If reactions were observed at the 72 hour observation, these were re-evaluated at 96 hours.

Study Group

81F/31M; age range 19-69 years

Vehicle

ethanol:diethyl phthalate (1:3)

Remarks – Method

Occluded. The test substance was spread on a 3.63 cm^2 patch. Information on negative control trial was not provided.

RESLUTS

Remarks – Results

103/112 subjects completed the study. Nine subjects discontinued with the study for reasons unrelated to the test substance.

During induction, a female exposed to 16% of the test substance showed raised skin (papules) at the 4th application and barely perceptible erythema at the 5-7th applications. The symptom was resolved at the 8th application.

No other adverse responses were noted at induction and challenge with the test substance at 16% concentration.

CONCLUSION The notified chemical was non-sensitising at 16% concentration under the conditions of the test.

TEST FACILITY CRL (2016)

B.4. Genotoxicity – Bacteria

TEST SUBSTANCE Notified chemical

METHOD OECD TG 471 Bacterial Reverse Mutation Test
Plate incorporation (Test 1) and pre incubation (Test 2) procedure

Species/Strain *Salmonella typhimurium*: TA1535, TA1537, TA98 and TA100
Escherichia coli: WP2uvrA

Metabolic Activation System S9 mix from phenobarbitone/ß-naphthoflavone induced rat liver

Concentration Range in Main Test
Test 1
a) With metabolic activation: 50, 150, 500, 1,500 and 5,000 µg/plate
b) Without metabolic activation: 50, 150, 500, 1,500 and 5,000 µg/plate

Test 2
a) With metabolic activation: 15, 50, 150, 500, 1,500 and 5,000 µg/plate
b) Without metabolic activation: 15, 50, 150, 500, 1,500 and 5,000 µg/plate

Vehicle DMSO

Remarks – Method Positive controls:
with S9-mix: 2-aminoanthracene (TA100, TA1535, TA1537 and WP2uvrA) and benzo(a)pyrene (TA98)
without S9-mix: *N*-ethyl-*N'*-nitro-*N*-nitrosoguanidine (TA100, TA1535 and WP2uvrA); 4-nitroquinoline-1-oxide (TA98) and 9-aminoacridine (TA1537).

A preliminary toxicity test was conducted on tester strains TA100 and WP2uvrA at a dose range of 0.15-5,000 µg/plate.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 5,000	≥ 5,000	≥ 5,000	Negative
Test 2		≥ 1,500	≥ 5,000	Negative
Present				
Test 1	> 5,000	> 5,000	≥ 5,000	Negative
Test 2		≥ 5,000	≥ 5,000	Negative

Remarks – Results No biologically relevant increases in revertant colony numbers of any of the tester strains were observed during the tests in either the presence or absence of metabolic activation.

The positive controls induced a significant increase of revertant colonies during the study indicating the validity of the test system.

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

TEST FACILITY Harlan (2013a)

B.5. Genotoxicity – *In vitro* chromosome aberration

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 473 *In vitro* Mammalian Chromosome Aberration Test (1997)
Species/Strain	Human
Cell Type/Cell Line	Lymphocytes
Metabolic Activation System	S9 mix from phenobarbitone/ß-naphthoflavone induced rat liver
Vehicle	Eagle's minimal essential medium with HEPES buffer (MEM)
Remarks – Method	A preliminary experiment (at a concentration range of 19.53-5,000 µg/mL) was conducted to determine the dose range for the main test.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 300*, 600*, 1,200*, 1,600, 2,000 and 2,400	4 h	20 h
Test 2	0*, 75, 150, 300*, 450*, 600* and 1,200*	24 h	-
Present			
Test 1	0*, 300*, 600*, 1,200*, 1,600, 2,000 and 2,400	4 h	20 h
Test 2	0*, 150, 300*, 600*, 1,200*, 1,500* and 1,800	4 h	20 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	≥ 2,500	≥ 1,200	≥ 300	Negative
Test 2	≥ 625	≥ 1,200	≥ 600	Negative
Present				
Test 1	≥ 2,500	≥ 1,600	≥ 300	Negative
Test 2	Not conducted	≥ 1,800	≥ 1,200	Negative

Remarks – Results	No biologically relevant increases in revertant colony numbers of any of the tester strains were observed during the test in either the presence or absence of metabolic activation. The positive and vehicle controls gave satisfactory responses confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic to human lymphocytes treated *in vitro* under the conditions of the test.
TEST FACILITY	Harlan (2013b)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready Biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	Acetone
Analytical Monitoring	Chemical Oxygen Demand (COD)
Remarks – Method	No significant deviations from the test guidelines were reported. A stock solution was made by dissolving 0.578 of test substance in 50 mL acetone. A test concentration of 21.3 mg/L and 53 .2 mg/L were prepared by adding 40 µL and 100 µL of stock solution into test tubes. The solvent was evaporated and 2 mL of deionized water was added.

RESULTS

Test Substance		*Aniline*	
Day	*% Degradation*	*Day*	*% Degradation*
7	23.2	7	58.4
14	28.9	14	74.7
21	31.7	21	97.3
28	32.9	28	98.3

Remarks – Results	All validity criteria for the test were satisfied. The percentage degradation of the reference compound, aniline 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 pH value of the content in the test system was maintained between 6.22 and 7.44. The total oxygen uptake in the inoculum blank was 22.3 mg O_2/L at the end of the study. The degree of degradation of the test substance after 28 days was 32.9%.
CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	NIES (2018a)

C.2. Ecotoxicological Investigations

C.2.1. Acute Toxicity to Fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test - Semi static
Species	*Gobiocypris rarus* (Rare minnow)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	134-142 mg $CaCO_3$/L
Analytical Monitoring	Ultra-Performance Liquid Chromatography (UPLC)
Remarks – Method	No significant deviations from the test guidelines were reported. Based on a range finding test, a water accommodated fraction (WAF) test solution with a loading rate of 100 mg/L was prepared. This mixture was stirred for 24 hours. The saturated solution was left for 1 hour and was filtered through 0.45 µm membrane, to give a stock solution of the test item. This stock solution was then further diluted to provide the remaining test

concentrations. The mean measured concentrations of 10%, 20%, 40%, 60%, 80% and 100 % of the stock solution was 1.87, 3.72, 7.51, 11.2, 15.0 and 18.7 mg/L, respectively. The analytical results showed that the concentration of the test substance was consistent in the test medium throughout the 96-hour test period (deviation within 20%). Thus a semi-static conditions (24 h renewal) procedure was applied. The 96 h-LC50 of the test substance to fish was based on the mean measured concentration, of daily measurements. A positive control ($K_2Cr_2O_7$) was run.

RESULTS

Concentration		*Number of Fish*	*Mortality*			
Nominal (%)	*Mean measured concentration(mg/L)*		*24 h*	*48 h*	*72 h*	*96 h*
Control	ND	10	0	0	0	0
10%	1.87	10	0	0	0	0
20%	3.72	10	0	0	2	3
40%	7.51	10	3	4	5	7
60%	11.2	10	6	8	10	10
80%	15	10	10	10	10	10
100%	18.7	10	10	10	10	10

ND: not detected

LC50 5.06 mg/L at 96 hours

Remarks – Results The statistical method for calculating the LC50 was not specified.
All validity criteria were met. During the test period, the pH values of the control mediums and test mediums were between 7.71 and 7.86, and the Dissolved Oxygen (DO) values varied from 88% - 97% of the air saturation. The deviation from the nominal concentration was greater than 20% and therefore the results are based on mean measured concentration. The 24 h LC50 of the positive control was 310 mg/L and is considered to be within the accepted range.

CONCLUSION The notified chemical is toxic to fish.

TEST FACILITY NIES (2018b)

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