Australian Government
Department of Health
Australian Industrial Chemicals Introduction Scheme

Oils, Schinus terebinthifolius

Assessment Statement (CA09525)

08 June 2022

Table of contents

AICIS assessment statement

Chemical in this assessment

Name	CAS registry number
Oils, Schinus terebinthifolius	949495-68-5

Reason for the assessment

An application for an assessment certificate under section 31 of the *Industrial Chemicals Act 2019* (the Act)

Certificate Application Type

Very low to low risk

Based on the introduction, use and end use information described in the application, the human health and environment exposure bands of the introduction are 3 and 2 respectively [table item 5 Clause 1 and table item 2 Clause 3, Schedule 1 of the *Industrial Chemicals (General) Rules 2019* (the Rules)]. The assessed chemical has hazard characteristics in human health hazard bands A and B (table items 16 and 12, clause 2, Schedule 1 of the Rules), and environment hazard band B (table item 8, clause 4, Schedule 1 of the Rules). In accordance with item 10 subsection 28(1) and item 12 subsection 29(1) of the Rules, the indicative human health risk and environment risk for the proposed introduction are both low risk.

Defined scope of assessment

The chemical has been assessed:

- as an essential oil of Schinus Terebinthifolius (Anacardiaceae) obtained from red berries by supercritical carbon dioxide extraction; and
- as imported in fragrance formulations at less than or equal to 1 tonne/annum in volume and at less than or equal to 1% in concentration, with reformulation and/or repackaging occurring in Australia; and
- for an end use as a fragrance ingredient in
    - fine fragrances and air care products at concentrations of 1% or less,
    - deodorants at concentrations of 0.3% or less, and
    - other consumer household and cosmetic products at concentrations of 0.2% or less.

Summary of assessment

Summary of introduction, use and end use

The chemical will be imported into Australia at up to 1% concentration in fragrance blends. Reformulation and repackaging processes will occur in Australia by downstream industrial users to produce a wide range of household and cosmetic products for consumer use that may

include laundry or dishwashing detergents, all-purpose cleaners, air care products, fine fragrances, deodorant products, leave on or rinse off cosmetics and hair care products. The use concentrations of the chemical are 0.2% or less in typical consumer products, 0.3% or less in deodorant products, and 1% or less in fine fragrances and air care products. The end use products containing the chemical will be widely used by professional workers including cleaners and beauty salon workers as well as public consumers.

Human health

Summary of health hazards

The assessed chemical is an unknown variable composition or biological (UVCB) substance with multiple components (see **Supporting information**). Based on the available information, the critical health effects for risk characterisation are skin sensitisation. The assessed chemical may also cause aspiration hazard if swallowed and enters airways.

The chemical tested positive in a local lymph node assay (LLNA) for skin sensitisation with EC3 at 22.3%. In a human repeat insult patch test (HRIPT), the assessed chemical at 10% concentration did not elicit skin irritation or sensitisation.

Based on the information available on the components of the assessed chemical, it is likely to oxidise over time, increasing the skin sensitising potency. The assessed chemical may also cause sensory irritation and respiratory effects.

No repeat dose toxicity data are provided on the assessed chemical. Based on the concentration of a component chemical, bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl- (CAS No. 80-56-8), classified with Category 2 specific target organ toxicity (repeated exposure) (STOT-RE) in Hazardous Chemical Information System (HCIS), the assessed chemical may cause harmful effects from repeated exposure if the component chemical exists at or above 10% concentration. This is based on the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) cut-off concentration for chemicals classified with Category 2 STOT-RE (UNECE 2017).

Based on the available data the assessed chemical is

- of low acute toxicity;
- not expected to be severely irritating to skin and eyes;
- not expected to be genotoxic.

Hazard classifications relevant to worker health and safety

The assessed chemical satisfies the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant to human health and safety as follows.

Health hazard	Hazard category	Hazard statement
Skin sensitisation	Skin Sens. 1B	H317: May cause an allergic skin reaction
Aspiration hazard	Asp. Tox. 1	H304: May be fatal if swallowed and enters airways

Physical hazard	Hazard category	Hazard statement
Flammable liquids	Flam. Liquid 3	H226: Flammable liquid and vapour

The assessed chemical contains bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl- in a typical concentration range of 8 – 23%. As this component is Category 2 STOT-RE, if its concentration within the assessed chemical is equal to or greater than 10% the assessed chemical also satisfies the GHS criteria for classification of Category 2 STOT-RE with a hazard statement of H373 - May cause damage to organs through prolonged or repeated exposure.

Summary of health risk

Workers

When introduced and used in the proposed manner, workers may be exposed to the chemical at less than or equal to 1% concentration while reformulating or repackaging imported fragrance blends containing the chemical into cosmetic and household products. Professional end use workers may have potential for repeated exposure to the chemical at less than or equal to 1% concentration. The assessed chemical in neat form is a flammable liquid with aspiration hazard and a Category 1B skin sensitiser. The neat form of the assessed chemical will not be imported. Specific risk management measures (see **means for managing risks** section) are required to manage the skin sensitisation risks to workers handling the assessed chemical at 1% concentration. No specific controls are required for workers applying end use products to customers.

Public

When introduced and used in the proposed manner, the public will be widely and repeatedly exposed to the chemical at concentrations less than or equal to 1% while using the household and cosmetic products containing the chemical. Based on our quantitative risk assessment (QRA):

- The assessed chemical is unlikely to cause systemic effects upon repeated exposure at low concentrations as proposed for use in the household and cosmetic products;
- Skin sensitisation associated with the use of the assessed chemical in a single consumer product at a low concentration is unlikely to occur.

Overall if the assessed chemical is introduced and used in accordance with the terms of the assessment certificate, no risks are identified for public health during this assessment that require specific risk management measures.

Environment

Summary of environmental hazard characteristics

According to domestic environmental hazard thresholds and based on the available data the chemical is:

- Not Persistent (not P)
- Bioaccumulative (B)
- Not toxic (not T)

Environmental hazard classification

The assessed chemical is formally classified under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (7th ed, UNECE 2017) as Acute Category 2 (H401) and Chronic Category 2 (H410) based on the toxicity to aquatic invertebrates. The EC50 values for the chemical are in the range of 1-10 mg/L and the chemical is not considered to be rapidly degradable in aquatic ecosystems for the purposes of this aquatic hazard classification.

Environmental hazard	Hazard category	Hazard statement
Acute Aquatic	Acute aq. – Cat. 2	H401: Toxic to aquatic life
Chronic Toxicity	Chronic aq. – Cat. 2	H411: Toxic to aquatic life with long lasting effects

Summary of environmental risk

Based on the end use as a fragrance in cosmetics and other consumer products, the majority of the assessed chemical is expected to be released into sewage treatment plants (STPs). The calculated aquatic environmental risk quotient for the assessed uses of the chemical is less than or equal to 0.01.

The assessed chemical has no demonstrated degradability, but is a biological chemical, and has the potential to bioaccumulate. The assessed chemical is not toxic to aquatic organisms under domestic criteria.

As the assessed chemical is not PBT it is unlikely to have unpredictable long-term effects and its risk may be estimated by the risk quotient method (RQ = PEC ÷ PNEC, see **Supporting information**). Based on the RQ < 1, the assessed chemical is unlikely to cause environmental risks.

Means for managing risks

Workers

Recommendation to Safe Work Australia

- It is recommended that Safe Work Australia (SWA) update the *Hazardous Chemical Information System* (HCIS) to include classifications relevant to work health and safety.

Information relating to safe introduction and use

- The information in this statement includes recommended hazard classifications and should be used by a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.
- The following control measures could be implemented to manage the risks arising from potential exposure to the assessed chemical during formulation of products:
    - Use of engineering controls such as
        - Enclosed and automated processes

    - Use of safe work practices to
        - Avoid contact with skin or eyes
        - Avoid spills
    - Use of personal protective equipment (PPE) including
        - Impervious gloves
        - Face mask
        - Protective clothing

- Model codes of practice, available from the Safe Work Australia website, provide information on how to manage the risks of hazardous chemicals in the workplace, prepare an SDS and label containers of hazardous chemicals. Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

Conclusions

The conclusions of this assessment are based on the information described in this statement. Considering the proposed means of managing risks, the Executive Director is satisfied that when the assessed chemical is introduced and used in accordance with the terms of the assessment certificate the human health and environment risks can be managed within existing risk management frameworks. This is provided that all requirements are met under environmental, workplace health and safety, and poisons legislation as adopted by the relevant state or territory, and the proposed means for managing the risks identified during this assessment are implemented.

Supporting information

Chemical identity

Synonyms	Pepper Pink CO2 Extr (trade name on SDS)
Structural formula	Unspecified
Molecular formula	Unspecified
Molecular weight (g/mol)	134 g/mol – 204 g/mol
Chemical description	Unknown variable composition or biological (UVCB) substance

The assessed chemical extracted from the berries by critical CO_2 extraction is a UVCB substance containing the following identifiable components:

Chemical Name	CAS No.	Typical Conc. (%)	Range Conc. (%)
Bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl-	80-56-8	14.51	8 - 23
Bicyclo[3.1.0]hexane, 4-methylene-1-(1-methylethyl)-	3387-41-5	3.45	0 - 5
1,6-Octadiene, 7-methyl-3-methylene-	123-35-3	1.95	0 - 5
1,3-Cyclohexadiene, 2-methyl-5-(1-methylethyl)-	99-83-2	27.97	12 - 35
Bicyclo[4.1.0]hept-3-ene, 3,7,7-trimethyl-	13466-78-9	10.76	1 - 29
Benzene, 1-methyl-4-(1-methylethyl)-	99-87-6	2.25	0 - 5
Cyclohexene, 3-methylene-6-(1-methylethyl)-	555-10-2	6.39	0 - 10
Cyclohexene, 1-methyl-4-(1-methylethenyl)-	138-86-3	7.39	0 - 14
Bicyclo[7.2.0]undec-4-ene, 4,11,11-trimethyl-8-methylene-, (1*R*,4*E*,9*S*)-	87-44-5	2.4	0 - 6
1,6-Cyclodecadiene, 1-methyl-5-methylene-8-(1-methylethyl)-, (1E,6E,8S)-	23986-74-5	11.63	3 - 14
Cyclohexane, 1-ethenyl-1-methyl-2-(1-methylethenyl)-4-(1-methylethylidene)-	3242-08-8	1.44	0 - 3

The UVCB substance also contains unknown compounds at approximately 10% by weight.

Relevant physical and chemical properties

Physical form	Clear yellow liquid

Freezing Point	< -76 °C
Boiling Point	161 – 271°C with 60% of the components at about 177 °C
Relative Density $D^{20}/_4$	0.87
Dynamic Viscosity	1.86 mPa.s at 25 °C (equivalent to kinematic viscosity of 2.14 mm^2/s)
Flash Point*	42 °C (closed cup)
Auto-ignition point	235 °C at about 1 atm
Vapour pressure	186.9 Pa at 25 °C
Water solubility	61.4 mg/L at 25 °C
Ionisable in the environment?	No
log K_{ow}	≥ 4.8 – ≤ 5.7
Log K_{oc}	≥ 3.03 – ≤ 4.30

* Based on GHS, a liquid with a flash point ≥ 23 °C and ≤ 60 °C is a Category 3 flammable liquid.

Introduction and use

The chemical will be imported at up to one tonne per year into Australia at a concentration of 1% or less in fragrance formulations. These formulations will be blended by downstream industrial users into a wide range of household and cosmetic products. Consumer products likely to contain the assessed chemical as a fragrance ingredient include:

- Instant action, continuous action, and motor vehicles air fresheners
- Waxes and polishes
- Leather and textile treatment products
- Liquid, foam and powder cleaners
- Laundry and dishwashing detergents
- Stain removers
- Soaps
- Perfumes and body sprays
- Hair and nail care products
- Rinse-off and leave-on cosmetics

There will be frequent and widespread consumer uses of household and cosmetic products containing the assessed chemical at a maximum concentration of 1%.

Human exposure

Workers

Workers in downstream reformulation and repackaging facilities may be exposed to the assessed chemical at a maximum concentration of 1% during operations.

Professional service end use workers may be exposed to the chemical in services where washing, cleaning, polishes, and cosmetic applications occur. These are likely to include beauty salons, hairdressers, and professional cleaning services. Dermal exposure of workers to the assessed chemical at ≤1% concentration may be frequent if PPE is not used or used improperly. Ocular and respiratory exposure to the chemical is also possible, especially from end use spray products.

Public

Dermal exposure of the public to the assessed chemical at ≤ 1% concentration will be wide-spread and frequent across a variety of possible household and cosmetic products. Incidental oral, ocular or respiratory exposure to the chemical at a maximum concentration of 1% may also be possible.

Data on typical use patterns of product categories in which the assessed chemical may be used are shown in the following tables and these are based on information provided in various literatures (SCCS 2012; Cadby *et al*. 2002; ACI 2010; Loretz *et al*. 2006). For the purposes of exposure assessment, Australian use patterns for the various product categories are assumed to be similar to those in Europe. A dermal absorption (DA) rate of 100% was assumed for the assessed chemical for calculation purposes. For the inhalation exposure assessment, a 2-zone approach was used (Steiling *et al*. 2014; Rothe *et al*. 2011; Earnest Jr. 2009). An adult inhalation rate of 20 m^3/day (enHealth 2012) was used and it was conservatively assumed that the fraction of the assessed chemical possibly inhaled is 50%. A lifetime average female body weight (BW) of 70 kg (enHealth 2012) was used for calculation purposes.

Cosmetic products (dermal exposure)

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (mg/kg bw/day)
Body lotion	7820	0.2	1	0.2234
Face cream	1540	0.2	1	0.0440
Hand cream	2160	0.2	1	0.0617
Fine fragrances	750	1.0	1	0.1071
Deodorant (non-spray)	1500	0.3	1	0.0643
Deodorant (spray)	1430	0.3	1	0.0613
Shampoo	10460	0.2	0.01	0.0030
Conditioner	3920	0.2	0.01	0.0011

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (mg/kg bw/day)
Shower gel	18670	0.2	0.01	0.0053
Hand soap	20000	0.2	0.01	0.0057
Hair styling products	4000	0.2	0.1	0.0114
Facial Cleanser	800	0.2	0.01	0.0002
Total				**0.5887**

C = maximum intended concentration of assessed 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	0.2	0.95	10	0.0062
Fabric softener	90	0.2	0.95	10	0.0024
Total					**0.0087**

C = maximum intended concentration of assessed chemical
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	0.2	1980	0.01	0.01	0.007	0.0001
Dishwashing liquid	3	0.2	1980	0.009	0.01	0.03	0.0005
All-purpose cleaner	1	0.2	1980	1	0.01	0.007	0.0040
Total							**0.0045**

C = maximum intended concentration of assessed chemical
Daily systemic exposure = (Frequency × C × Contact area × Product Use Concentration × Film Thickness on skin × Time Scale Factor × DA)/BW

Hair spray (inhalation exposure)

Amount of hairspray applied	9.89	g/day
Maximum intended concentration of the chemical	0.2	%

Inhalation rate of the user	20	m^3/day
Exposure duration in zone 1	1	minutes
Exposure duration in zone 2	20	minutes
Fraction inhaled by the user	50	%
Volume of zone 1	1	m^3
Volume of zone 2	10	m^3
Daily systemic exposure	**0.0059**	mg/kg bw/day

C = maximum intended concentration of assessed chemical
Total daily systemic exposure = Daily systemic exposure in zone 1 [(amount × C × inhalation rate × exposure duration (zone 1) × fraction inhaled)/(volume (zone 1) × body weight)] + Daily systemic exposure in zone 2 [(amount × C × inhalation rate × exposure duration (zone 2) × fraction inhaled)/(volume (zone 2) × body weight)]

The worst-case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above tables that contain the assessed chemical at the maximum intended concentrations specified in various product types. This would result in a combined internal dose of 0.6077 mg/kg bw/day for the assessed chemical. It is acknowledged that inhalation exposure to the assessed 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 hair spray inhalation exposure assessment parameters, and the aggregate exposure from use of the dermally applied products, which assumes a conservative 100% dermal absorption rate, is sufficiently protective to cover additional inhalation exposure to the assessed chemical from use of other spray cosmetic and household products with lower exposure factors (e.g. air fresheners).

Health hazard information

Acute toxicity

Oral

In an acute toxicity study (OECD TG 423) the assessed chemical was administered via oral gavage to 6 female rats at 2000 mg/kg bw. Three test animals were sedated for up to 5 hours after the administration. No pre-mature deaths occurred during the study. On day 1 of the observation period, all rats displayed signs of hunched posture and slightly ruffled fur. On days 2 to 4, light beige faeces were observed. The body weight of the test animals was within the common range recorded for the strain and age. No macroscopic findings were recorded at necropsy.

The median lethal dose (LD50) was reported to be greater than 2000 mg/kg bw in rats. Based on the available data, the test substance may be of low acute oral toxicity.

Dermal

No acute dermal toxicity data were submitted.

In a local lymph node assay (LLNA) conducted to determine the skin sensitisation potential (see below), the assessed chemical was pre-tested on two mice for dose determination purposes by topical application of 10% and 20% concentrations on one mouse, and 50% and 100% concentrations on the other, at the dorsum of each ear lobe on three consecutive days. The mouse tested using 50% and 100 % concentrations on separate ears died after the second topical application. It was unclear what caused the mortality. However, a second pre-test using the assessed chemical was then performed with 50% concentration on each ear and did not induce systemic toxicity or mortality.

Corrosion/Irritation

Skin irritation

In an in vitro skin irritation study conducted using the reconstructed human epidermis test method (OECD TG 439), the assessed chemical was tested in its neat form without dilution. After a 15-minute exposure period and a 42-hour post-exposure incubation period, the results indicated that the relative mean viability of the treated tissues was 95.9 ± 11.5% when compared to the negative control tissues. The quality criteria required for acceptance of the results were satisfied in the study.

Based on the study results, the assessed chemical is considered a non-irritant to skin, requiring no GHS classification.

Eye irritation

In a bovine corneal opacity and permeability (BCOP) assay [INVITTOX protocol 98 UK (1994), similar to OECD TG 437], the assessed chemical was tested for eye irritation potential in the neat form without dilution. After a 10 min exposure, the test substance did not cause any opacity or permeability of the corneas compared to the negative controls. The positive control had a calculated in vitro score of 45 and did not meet the minimum required in vitro score of 55, however, the study was considered acceptable by the study authors. The in vitro score of the assessed chemical was determined to be 0.13. An in vitro score between 0 and 3 is considered non-irritating according to the study protocol.

Based on the study results, the assessed chemical was not considered to be an eye irritant, requiring no GHS classification.

Respiratory irritation

No data are available for the assessed chemical. The assessed chemical contains several terpene type components. Sensory irritation and respiratory symptoms are reported in humans following exposure to mixed monoterpenes (NICNAS 2002; NICNAS 2018a; NICNAS 2018b).

Sensitisation

Skin sensitisation

In a local lymph node assay (LLNA) for skin sensitisation (OECD TG 429), the assessed chemical was topically administered at 10%, 25%, and 50% concentrations to the ears of mice. No sign of systemic toxicity or excessive local skin irritation were noted at the concentrations tested. However, the pre-test conducted with 2 mice caused mortality of one when the chemical was applied at one ear at 50% concentration and the other at 100% concentration after the

second application on day 2. The cause of the death was not reported. The test concentration of 100% was therefore avoided in the main study.

The resulting stimulation index (SI) for 10%, 25% and 50% (w/v) in acetone/olive oil 4:1 was 1.62, 3.30 and 4.77, respectively. The EC3 was then calculated to be 22.3%. Based on GHS criteria for classification, the assessed chemical is determined to be a Category 1B skin sensitiser.

The assessed chemical contains several terpene type components. Autoxidation and formation of autoxidation products of these components are also known to cause sensitisation (AICIS 2022; NICNAS 2002; NICNAS 2018a; NICNAS 2018b; NICNAS 2018c).

In a human repeat insult patch test (HRIPT) (Shelanski Method) with the assessed chemical at 10% concentration, 112 subjects participated in the study. Among them 7 subjects discontinued for reasons unrelated to the test material application and 105 subjects completed. The assessed chemical was administered at 10% concentration in ethanol and diethyl phthalate to the upper back of each subject with a covered patch area of 3.63 cm^2. During the induction phase the assessed chemical was topically applied 9 times over a 3 week period. During the challenge phase, the assessed chemical was applied to new skin sites. The dermal observations in both the 105 completed subjects and the 7 discontinued subjects recorded no observable skin reactions at any point during the study. The study authors concluded that up to 10% concentration, the assessed chemical did not elicit skin irritation or sensitisation.

Repeat dose toxicity

No repeat dose toxicity data on the assessed chemical were submitted.

In the absence of data on the UVCB chemical, the applicant provided supporting evidence for 11 major chemical components identified in the UVCB. No-observed-adverse-effect levels (NOAELs) were provided for 10 of the components, ranging from 16.67 to 1033 mg/kg bw/day.

The neat form of the assessed chemical contains 1,6-octadiene, 7-methyl-3-methylene- (CAS No. 123-35-3) in a concentration range of 0 – 5%. A 90 day repeated dose toxicity study conducted in rats on this component used 250 mg/kg bw/day as the lowest treatment dose and there were systemic toxicity effects reported at this dose level (AICIS 2022). A NOAEL could not be established for the component, and the lowest observed adverse effect level (LOAEL) was reported as 250 mg/kg bw/day.

The neat form of the assessed chemical also contains bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl- (CAS No. 80-56-8) in a concentration range of 8 – 23%. This component is listed on HCIS as a Category 2 STOT-RE.

Based on the summarised information provided by the applicant, some of other components of the chemical have also been reported to have systemic effects in rats or mice at high dose levels through prolonged or repeated administrations that might include reproductive or developmental, liver and bodyweight effects.

Genetic toxicity

In a bacterial reverse mutation assay (OECD TG 471) the assessed chemical was tested using *Salmonella typhimurium* (TA 1537, TA 98, TA 1535, TA 100) and *Escherichia coli* (WP2 uvrA) strains at concentrations of 3, 10, 33, 100, 333, 1000, 2500, and 5000 µg/plate. The test substance reduced background growth for *S. typhumurium* strains from as low as 100 µg/plate,

showing cytotoxicity. The number of revertant colonies decreased due to the cytotoxicity. However, *E. coli* strains were unaffected. The results indicated that there was no significant increase in revertant colonies compared to the negative controls either with or without metabolic activation. There was also no biologically relevant dose response observed in the study for the mutation rate. Based on the results, the assessed chemical was not considered to be mutagenic.

No other genotoxicity data were provided. Several terpene type components of the chemical are not considered to be genotoxic (AICIS 2022; NICNAS 2002; NICNAS 2018a; NICNAS 2018b; NICNAS 2018c).

Carcinogenicity

One of the chemical components, 1,6-Octadiene, 7-methyl-3-methylene- (CAS No. 123-35-3), is present in the assessed chemical at 0 to 5% concentration range. The International Agency for Research on Cancer has classified this component as 'possibly carcinogenic to humans' (Group 2B) (IARC 2019). However, an evaluation for the component by AICIS concluded that the available data are insufficient to determine whether the chemical has carcinogenic potential relevant to humans (AICIS 2022).

There was clear evidence of carcinogenic activity of the chemical component d-limonene (CAS No. 138-86-3) in male rats, based on a dose-related increase in the incidence of hyperplasia and adenoma/adenocarcinoma in renal tubular cells. However, there was no evidence of carcinogenicity in female rats or in male and female mice. The carcinogenic response in the kidney of male rats has been linked to a unique renal perturbation involving $\alpha 2\mu$-globulin which is known to be not relevant to humans (NICNAS 2002).

Aspiration hazard

The measured dynamic viscosity of the assessed chemical at 25 °C is 1.86 mPa.s which is equivalent to a kinematic viscosity of 2.14 mm^2/s given the relative density $D^{20}/_4$ at 0.87. The kinematic viscosity of the chemical at 40 °C is not recorded, however it is estimated to be below 20.5 mm^2/s. Based on GHS criteria, a hydrocarbon compound with a kinematic viscosity ≤ 20.5 mm^2/s at 40 °C is classifiable as a Category 1 aspiration hazard.

Health risk characterisation

No repeated dose toxicity data are provided specifically for the assessed chemical (UVCB) and it contains unknown components at approximately 10% by weight. If the assessed chemical is imported at a maximum concentration of 1% as proposed, the unknown components in the imported fragrance blends can be up to 0.1%. Potential adverse health effects from repeated exposure to the assessed chemical at introduction or use concentrations above 1% cannot be ruled out.

Workers

The assessed chemical in its neat form is a flammable liquid. Based on its viscosity, it may present an aspiration hazard. However, the assessed chemical will only be imported into Australia in fragrance blends at ≤ 1% concentration for reformulation into consumer products.

The assessed chemical is a Category 1B skin sensitiser and potentially a Category 2 STOT-RE that may cause harmful effects following repeated exposure. To mitigate relevant risks,

workers at the reformulation or repackaging sites are expected to use appropriate PPE with necessary control measures in place.

Professional end users, such as cleaners and beauty salon workers, may have potential for repeated or prolonged exposure to the assessed chemical at a maximum concentration of 1% when using the end use products containing the chemical. Certain level of PPE may be used by these workers and the extent of the exposure to the chemical is expected to be similar to the public consumers (see below).

Public

A QRA was performed using the NOAEL or LOAEL values of each component and the total daily systemic internal doses for public exposure (see **Human exposure** section). The margin of exposure (MOE) was calculated for each component in relation to the proportion of each component in the assessed chemical introduced. The MOE for all major chemical components was above 100. A MOE greater than 100 is generally considered acceptable for human health risk assessment purposes. The assessed chemical is unlikely to cause systemic effects upon repeated exposure at low concentrations as proposed for the assessed uses in the household and cosmetic products.

The assessed chemical is not considered as a skin or eye irritant when introduced and used at a maximum concentration of 1%. However, the chemical is a Category 1B skin sensitiser (EC3 = 22.3%). In a HRIPT, the assessed chemical at 10% concentration was determined as not eliciting a sensitisation response. Consideration of the details of the two submitted studies allowed the derivation of an Acceptable Exposure Level (AEL) of 35.95 µg/cm^2/day for consumers using an overall safety factor of 100. Based on the QRA calculations, this AEL was considered to be greater than or equal to each of the individual consumer exposure levels (CELs) for various household and cosmetic products with intended maximum use concentrations as proposed in the application. Since the AEL is greater than or equal to CEL, induction of skin sensitisation associated with the use of the assessed chemical in a single consumer product at a low concentration is unlikely to occur. However, it is acknowledged that consumers may be exposed to multiple products containing the assessed chemical, and a quantitative assessment based on aggregate exposure has not been conducted.

Environmental exposure

Releases of the assessed chemical to the environment are not expected during reformulation, transport or storage.

The assessed chemical is being introduced as a fragrance ingredient to be included in a range of products, resulting in a variety of potential exposure scenarios. As a fragrance ingredient, a proportion of the assessed chemical is anticipated to volatilise during use, but this proportion is not assumed to be significant for every use.

Use of the assessed chemical in air-care products will involve spraying of the product into the air, resulting in direct release of the assessed chemical into the air compartment.

Use of the assessed chemical in washing and cleaning products, and in cosmetic products is expected to result in the release of the products “down the drain” into sewerage treatment plants and aquatic environments.

Environmental fate

Partitioning

The assessed chemical is highly volatile and moderately water soluble. The assessed chemical has a high calculated log K_{OC} value (log K_{OC} = 3.03 – 4.30) and a high log K_{OW} range (log K_{OW} = 4.8 – 5.7). Therefore, the chemical is expected to partition to and become immobile in soils and sediments.

If the assessed chemical is released to water, the chemical is expected to partition primarily between the water and air, with some minor partitioning to sediments. A moderate fraction of the assessed chemical is expected to be released to air during STP treatment based on its moderate volatility (vapour pressure = 186.9 Pa). Similarly, a proportion of the assessed chemical in air care products is also expected to be released to air during use.

When released directly to the air, the assessed chemical is expected to completely stay within the air compartment.

Degradation

The assessed chemical is determined to be a biological chemical, according to the definition outlined in *Industrial Chemicals (General) Rules 2019* (the Rules), and is assumed to be not persistent.

Bioaccumulation

The assessed chemical has high log K_{OW} values ranging between 4.8 and 5.7. Therefore, based on the categorisation criteria the assessed chemical is expected to have the potential to bioaccumulate in organisms.

Predicted environmental concentration (PEC)

The predicted environmental concentrations (PEC) in water (receiving environments) have been conservatively calculated based on 100% release of the assessed chemical (from the introduction volume) into sewer systems nationwide over 365 days per annum. The extent to which the assessed chemical is removed from the effluent in STP processes is based on its physicochemical properties, modelled by SimpleTreat 3.0 (Struijs 1996) and is estimated to be 94%. Therefore 6% of the total introduction volume is estimated to be released to the aquatic environment. The calculation of the PEC is detailed in the table below:

Total Annual Import 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	24.386	Million
Removal within STP	94%	Mitigation
Daily effluent production	4,877	ML/day
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River	0.03	µg/L
PEC - Ocean	0.00	µg/L

Environmental effects

Effects on Aquatic Life

Acute toxicity

The following measured median effective loading (EL50) values for model organisms were supplied by the applicant:

Taxon	Endpoint	Method
Invertebrate	EL50 = 15 mg/L	*Daphnia magna* (water flea) Immobility OECD TG 202 Static Nominal concentration
Algae	ErL50 = 4.8 mg/L	*Pseudokirchneriella subcapitata* (green algae) Growth rate OECD TG 201 Static conditions Nominal concentration

Predicted No-Effect Concentration (PNEC)

A Predicted No-Effect Concentration (PNEC) was calculated based on the above acute endpoint for algae using an assessment factor of 500 as only two acute trophic endpoints are available (EPHC 2009). The resulting PNEC is 9.6 µg/L.

Environmental hazard categorisation

The categorisation of the environmental hazards of the assessed chemical according to domestic environmental hazard thresholds is presented below:

Persistence

Not persistent (Not P). Based on the assessed chemical meeting the definition of a biological chemical according to the Rules, the assessed chemical is not persistent.

Bioaccumulation

Bioaccumulative (B). Based on high measured log K_{OW} value indicating a potential to bioaccumulate, the assessed chemical is categorised as Bioaccumulative.

Toxicity

Not Toxic (Not T). Based on the two available ecotoxicity values above 1 mg/L, the assessed chemical is categorised as Not Toxic.

Environmental risk characterisation

The assessed chemical is not PBT and is hence unlikely to have unpredictable long-term effects (EPHC 2009). An estimate of risk may therefore be determined using the risk quotient method.

Based on the PEC and PNEC values determined above, Risk Quotients (RQ = PEC ÷ PNEC) have been calculated for release of the assessed chemical to water:

Compartment	PEC	PNEC	RQ
River	0.03 µg/L	9.6 µg/L	< 0.01
Ocean	0.001 µg/L	9.6 µg/L	< 0.01

For the river and ocean compartments, an RQ less than 1 indicates that the assessed chemical is unlikely to cause environmental risk based on estimated emissions, as environmental concentrations are below levels that are likely to cause harmful effects.

References

ACI (2010) Consumer Product Ingredient Safety, Exposure and risk screening methods for consumer product ingredients, 2nd Edition, American Cleaning Institute, Washington DC.

AICIS (Australian Industrial Chemicals Introduction Scheme) (2022). 1,6-Octadiene, 7-methyl-3-methylene- (myrcene) draft Evaluation Statement. Accessed April 2022.

Cadby PA, Troy WR, Vey MGH (2002) Consumer Exposure to Fragrance Ingredients: Providing Estimates for Safety Evaluation. Regulatory Toxicology and Pharmacology, 36: 246-252.

Earnest CW Jr. (2009) A Two-Zone Model to Predict Inhalation Exposure to Toxic Chemicals in Cleaning Products, MScEng thesis, The University of Texas at Austin.

enHealth (2012) Australian Exposure Factor Guide, companion document to: Environmental Health Risk Assessment: Guidelines for assessing human health risks from environmental hazards, EnHealth, Commonwealth of Australia.

EPHC (2009) Environment Protection and Heritage Council, Environmental Risk Assessment Guidance Manual for industrial chemicals, Prepared by: Chris Lee-Steere Australian Environment Agency Pty Ltd, February 2009. ISBN 978-1-921173-41-7.

IARC (International Agency for Research on Cancer) 2019. IARC Monographs Volume 119. Some chemicals that cause tumours of the urinary tract in rodents. Accessed September 2021.

Loretz L, Api AM, Barraj L, Burdick J, Davis de A, Dressler W, Gilberti E, Jarrett G, Mann S, Laurie Pan YH, Re T, Renskers K, Scrafford C, Vater S (2006) Exposure data for personal care products: Hairspray, spray perfume, liquid foundation, shampoo, body wash, and solid antiperspirant. Food and Chemical Toxicology, 44: 2008–2018

McWilliams P, Payne G. (2001) *Bioaccumulation Potential of Surfactants: A Review*. Royal Society of Chemistry & EOSCA, Manchester, United Kingdom.

NICNAS (National Industrial Chemicals and Assessment Scheme) (2002) Limonene Priority Existing Chemical Report No.22 (PEC-22). Accessed August 2021.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2018a). Terpinene, terpinolene and phellandrene: Human health tier II assessment. Accessed May 2022.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2018b). Alpha-pinene: Human health tier II assessment. Accessed May 2022.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2018c). Bicyclo[4.1.0]hept-3-ene, 3,7,7-trimethyl-: Human health tier II assessment. Accessed May 2022.

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

Safe Work Australia (2020) Code of Practice for Managing Risks of Hazardous Chemicals in the Workplace. Commonwealth of Australia.

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

Steiling W, Bascompta M, Carthew P, Catalano G, Corea N, D'Haese A, Jackson P, Kromidas L, Meurice P, Rothe H, Singal M (2014) Principle considerations for the risk assessment of sprayed consumer products. Toxicology Letters, 227:41-49.

Struijs J (1996) SimpleTreat 3.0: a model to predict the distribution and elimination of chemicals by sewage treatment plants, National Institute of Public Health and the Environment.

UNECE (United Nations Economic Commission for Europe) (2017) Globally Harmonized System of Classification and Labelling of Chemicals (GHS), Seventh Revised Edition, UNECE, accessed February 2022.