Australian Government
Department of Health and Aged Care
Australian Industrial Chemicals Introduction Scheme

Oils, sandalwood, santalene synthase-modified Rhodobacter sphaeroides-fermented, from D-glucose, oxidized

Assessment statement (CA09524)

14 December 2022

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AICIS assessment statement

Chemical in this assessment

Name	CAS registry number
Oils, sandalwood, santalene synthase-modified Rhodobacter sphaeroides-fermented, from D-glucose, oxidized	2576531-09-2

Reason for the assessment

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

Certificate Application Type

Health Focus

According to information submitted by the applicant and criteria in the *Industrial Chemicals (General) Rules 2019* and the Industrial Chemicals Categorisation Guidelines, this introduction is in the **assessed** category. The reason is that this introduction has **medium to high** indicative risk for **human health** because it is in:

- human health exposure band 4
- human health hazard band B

The introduction of this chemical has **low** indicative risk for the **environment** because it is in:

- environment exposure band 2
- environment hazard band C

Defined scope of assessment

The chemical has been assessed as a fragrance ingredient in finished products used by workers and consumers and the following:

- Imported up to 1 tonne per year
- Household products at a concentration up to 0.02%
- Cosmetics at a concentration up to 0.1%
- Fine fragrances at a concentration up to 0.18%
- Air care products at a concentration up to 2%

Summary of assessment

Summary of introduction, use and end use

The assessed chemical will not be manufactured in Australia. It will be imported into Australia as a component in formulated end use products. The imported end use products will contain

the assessed chemical at up to 0.02% in household products, up to 0.1% in cosmetics, up to 0.18% in fine fragrances and up to 2% in air care products.

Finished consumer products containing the assessed chemical at various concentrations will be packaged in containers suitable for retail sale.

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 data the assessed chemical in neat form is likely to be a skin irritant and a moderate skin sensitiser (see **Supporting information**) warranting hazard classification (see below).

The available toxicity data indicate that the assessed chemical:

- is likely to be of low oral toxicity; and
- is unlikely to be genotoxic.

No inhalation toxicity data were provided on the assessed chemical.

No data were provided for repeated dose toxicity of the assessed chemical. The assessed chemical is a santalol, with ~20% unknown components. Based on the evaluation on santalol and its related substances (NICNAS 2019), the assessed chemical is unlikely to cause adverse health effects from repeated exposure at concentrations up to 2% (maximum concentration in end use products). The unknown components of the assessed chemical will be negligible (at ~0.4% concentration) at the maximum use concentration of 2%.

Hazard classifications relevant for 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 for worker health and safety as follows. This does not consider classification of environmental hazards.

Health hazards	Hazard category	Hazard statement
Skin corrosion/irritation	Skin Irrit. 2	H315: Causes skin irritation
Skin sensitisation	Skin Sens. 1B	H317: May cause an allergic skin reaction

Summary of health risk

Public

When introduced and used in the proposed manner, there will be widespread and repeated exposure of the public to the assessed chemical at up to 0.18% concentration through the use of a wide range of cosmetic and household products containing the assessed chemical. The principal route of exposure will be dermal, while ocular and inhalation exposures are also possible, particularly from products applied by spray.

The assessed chemical in neat form is likely to cause skin irritation and is a moderate skin sensitiser. However, these effects are not expected at the proposed end use concentrations in end use products (supported by a quantitative assessment for sensitisation effects). The assessed chemical is not persistent in the environment and therefore, not expected to cause inhalation risk when used at up to 2% concentration in air care products.

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.

Workers

Exposure to the assessed chemical in end use products (at up to 0.18% concentration) may occur in professions where the services provided involve the application of cosmetic and personal care products to clients (e.g. hairdressers and workers in beauty salons) or the use of household products in the cleaning industry.

The frequency and extent of exposure of workers applying products to clients is similar to public exposure or lower if personal protective equipment (PPE) is used. No specific controls are required for workers applying end use products to customers.

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)
- Toxic (T)

Environmental hazard classification

The chemical satisfies the criteria for classification according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE 2017) as Acute Category 1 (H400) and Chronic Category 1 (H410) based on the invertebrate toxicity data. Considerations were also made for the rapid biodegradation and bioaccumulation potential of the assessed chemical.

Environmental Hazard	Hazard Category	Hazard Statement
Acute Aquatic	Acute aq. – Cat. 1	H400: Very toxic to aquatic life
Chronic Aquatic	Chronic aq. – Cat. 1	H410: Very toxic to aquatic life with long lasting effects

Summary of environmental risk

The assessed chemical will be introduced as a fragrance for use in cosmetic, air care and other consumer products. This use may result in the release of the assessed chemical to sewers, surface waters and directly to air.

The assessed chemical is readily degradable and is not persistent. The assessed chemical has potential for bioaccumulation and is toxic to aquatic organisms, according to domestic threshold values.

Although the assessed chemical has the potential for bioaccumulation and is toxic, it does not meet all three PBT criteria. Therefore, it is unlikely to have unpredictable long-term effects and its risk may be estimated by the risk quotient (RQ) method (see **Supporting information**). Based on calculated RQ values < 1, it is expected that the environmental risk from the introduction of the assessed chemical can be managed.

Means for managing risk

Workers

Recommendation to Safe Work Australia

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

Information relating to safe introduction and use

No specific recommendations for the introduction and use of the assessed chemical are required when the assessed chemical is introduced and used in accordance with the terms of the assessment certificate.

Environment

No specific recommendations for the use of the assessed chemical are required when the assessed chemical is introduced in accordance with the terms of the assessment certificate.

Conclusions

The conclusions of this assessment are based on the information described in this statement.

The Executive Director is satisfied that when the 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 of managing the risks identified during this assessment are implemented.

Note: Obligations to report additional information about hazards under section 100 of the *Industrial Chemicals Act 2019* apply.

Supporting information

Chemical identity

Chemical name	Oils, sandalwood, santalene synthase-modified Rhodobacter sphaeroides-fermented, from D-glucose, oxidized
CAS No.	2576531-09-2
Structural formula	Unspecified
Molecular formula	Unspecified
Molecular weight (g/mol)	Unspecified
Chemical description	Unknown variable composition or biological (UVCB) substance

The assessed chemical is the product of the fermentation of D-glucose using *Rhodobacter sphaeroides*, which is further treated using the process of chlorination, acetylation, hydrolysis, distillation and filtration. The resulting chemical is a UVCB substance containing the following identified components and approximately 20.2% unknown components:

Chemical Name	CAS No.	Typical Conc. (%)	Range Conc. (%)
2-Penten-1-ol, 2-methyl-5-[(1*S*,2*R*,4*R*)-2-methyl-3-methylenebicyclo[2.2.1]hept-2-yl]-, (2*E*)-	37172-32-0	5.5	5 - 6
2-Penten-1-ol, 2-methyl-5-[(1*S*,2*R*,4*R*)-2-methyl-3-methylenebicyclo[2.2.1]hept-2-yl]-, (2*Z*)-	77-42-9	19.1	19 - 20
2-Penten-1-ol, 2-methyl-5-[(1*R*,2*R*,4*S*)-2-methyl-3-methylenebicyclo[2.2.1]hept-2-yl]-, (2*Z*)-rel-	79081-90-6	10.2	10 - 11
2-Penten-1-ol, 5-[(1*R*,3*R*,6*S*)-2,3-dimethyltricyclo[2.2.1.02,6]hept-3-yl]-2-methyl-, (2*E*)-	14490-17-6	12	11 - 13
2-Penten-1-ol, 5-[(1*S*,5*S*,6*R*)-2,6-dimethylbicyclo[3.1.1]hept-2-en-6-yl]-2-methyl-, (2*Z*)-	88034-74-6	2.8	2 – 3
2-Penten-1-ol, 5-[(1*R*,3*R*,6*S*)-2,3-dimethyltricyclo[2.2.1.02,6]hept-3-yl]-2-methyl-, (2*Z*)-	115-71-9	30.2	30 - 31

Relevant physical and chemical properties

Physical form	Viscous yellow liquid
Glass transition temperature	- 55.5 °C
Boiling point	75.5 °C at 30 hPa
Density	979 kg/m^3 at 20 °C
Vapour pressure	3.3 hPa at 20 °C 4.2 hPa at 25 °C 12.5 hPa at 50 °C
Water solubility	19.4–35.7 mg/L at 20°C
Ionisable in the environment?	No
log K_{ow}	4.45–4.71
Flash point	154 °C
Autoignition temperature	243 °C
pH	5.2 ± 0.1
Kinematic viscosity	494 mm^3/s at 20 °C 94.8 mm^3/s at 40 °C
Dynamic viscosity	483 mPa*s at 20 °C 91.5 mPa*s at 40 °C

Human exposure

Workers

Professional End Use

Exposure to the assessed chemical in end use products at up to 0.18% concentration may occur in professions where the services provided involve the application of cosmetic and personal care products to clients (e.g. hairdressers and workers in beauty salons) or the use of household products in the cleaning industry. These products, depending on their nature, could be applied in a number of ways, such as by hand, using an applicator or sprayed.

The principal routes of exposure will be dermal and inhalation (for spray products), while ocular exposure is also possible from spay applications. Professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using the end use products containing up to 0.18%% of the assessed chemical.

Public

There will be widespread and repeated exposure of the public to the chemical at up to 0.18% concentration through the use of a wide range of cosmetic and household products. The principal route of exposure will be dermal, while ocular or inhalation exposure is also possible, particularly if the products are applied by spray. Inhalation exposure to end use products containing up to 0.18% of the assessed chemical (including fine fragrances, cosmetics and household products) is expected to be limited by the low concentrations. While air care products will contain the assessed chemical at up to 2% concentration, inhalation exposure is also expected to be limited given the assessed chemical is not persistent in the environment.

Health hazard information

Acute toxicity

In an acute oral toxicity study (OECD TG 423), six female Wistar rats (3 per group) were administered the assessed chemical via oral gavage at a dose of 2000 mg/kg bw. No mortalities were observed. Clinical signs of toxicity included an impaired general state and piloerection in one animal during 2-3 hours after administration. There were no macroscopic findings in any treated animals. The median lethal dose (LD50) was determined to be greater than 2000 mg/kg bw. Based on the results of this study, the assessed chemical is likely to be of low acute oral toxicity.

No acute dermal or inhalation toxicity data are provided for the assessed chemical.

Corrosion/Irritation

Skin corrosion/irritation

In an in vitro skin corrosion test using the EpiDerm™ reconstructed human epidermis tissue model (OECD TG 431), the undiluted assessed chemical was tested by a single topical application of 50 µL to a EpiDerm™ tissue. Two test substance-treated tissues were incubated for 3 minutes and 60 minutes. The relative mean viability of the test substance-treated tissues was 107.9% after 3 min exposure and 122.2% after 60 min exposure (not meeting the criteria for corrosive prediction of GHS Category 1 chemicals). Based on the results, the assessed chemical is not considered to be corrosive to the skin.

In an in vitro skin irritation test using the EpiDerm™ reconstructed human epidermis tissue model (OECD TG 439), the assessed chemical was tested by a single topical application of 30 µL undiluted test substance to a EpiDerm™ tissue. Three test substance-treated tissues were incubated for 1 hour. The relative mean viability of the test substance-treated tissues was 4.7% (below the cut-off value of ≤ 50% for the prediction of irritation) after 1-hour exposure period. Based on the results, the assessed chemical is considered to be irritating to the skin warranting a hazard classification for skin irritation (Category 2, H315: Causes skin irritation) according to GHS criteria.

Eye irritation

The assessed chemical was tested by a single topical application of 50 µL undiluted test substance to a reconstructed Human EpiOcular™ Cornea-like Epithelial Model (OECD TG 492) to determine whether it is not an eye irritant or requires classification for serious eye damage. The relative mean tissue viability obtained after 30 min exposure was 95.4%,

compared to the negative control tissues, meeting the criteria for no classification according to the TG (> 60%). Based on the results, the assessed chemical is not considered to be irritating to eyes.

Sensitisation

Skin sensitisation

The skin sensitisation potential of the assessed chemical was assessed using a local lymph node assay (LLNA) in mice (OECD TG 429). The mice were treated by daily application of 25 µL of the test substance at concentrations of 2.5%, 10% or 25% (in ethanol) to the dorsal surface of each ear for three consecutive days.

There were no signs of systemic toxicity and body weights were comparable to controls. The stimulation index (SI) at the 2.5%, 10% or 25% concentrations were 1.47, 3.52 and 6.70, respectively. The concentration of test substance expected to cause a 3-fold increase in ^{3}HTdR incorporation (EC3 value) was calculated (by linear interpolation) to be 8.1%. Based on the results of this study, the assessed chemical is a skin sensitiser requiring hazard classification for Skin Sensitisation (Cat 1B: H317: May cause an allergic skin reaction) according to GHS criteria.

Repeat dose toxicity

No repeat dose toxicity data on the assessed chemical were submitted. There are no suitable analogue data available for the assessed chemical (which is a santalol with ~20% unidentified components).

Genotoxicity

The assessed chemical was found to be non-mutagenic in a bacterial reverse mutation assay (OECD TG 471).

No genotoxicity data on chromosomal damage was submitted for the assessed chemical. A structurally related chemical, 2,5,7-octatrien-1-ol, 2,6-dimethyl-, 1-acetate (CAS No. 197098-61-6), was considered to be representative for santalen-14-ol (CAS No. 77-42-9 and 115-71-9) and reported to give no concern with respect to genotoxicity (EFSA 2013). As santalen-14-ol (CAS No. 77-42-9 and 115-71-9) are two main components of the assessed chemical and structurally similar to the other components of the assessed chemical, the assessed chemical is likely to be non-genotoxic.

Environmental exposure

The assessed chemical will be imported into Australia as a component of formulated end use products. No reformulation of the assessed chemical will occur in Australia. Significant releases of the assessed chemical to the environment are not expected during transport or storage.

The assessed chemical is a fragrance ingredient to be included in a range of products, resulting in a variety of potential exposure scenarios.

Use of the assessed chemical in cosmetic products, washing products and cleaning products is expected to result in the release of the assessed chemical “down the drain” and into the

sewers. Consequently, the assessed chemical will be treated at sewage treatment plants (STPs) before release to surface waters.

Use of the assessed chemical in air care products will result in direct release of the assessed chemical into the air compartment.

Environmental fate

Partitioning

The assessed chemical is moderately soluble in water (water solubility = 19.4–35.7 mg/L at 20˚C). If the assessed chemical is released to surface water, a proportion of the assessed chemical is expected to remain in the water compartment and a proportion of the chemical is expected to partition to sediments based on its moderate water solubility and high log K_{OW} value (log K_{OW} = 4.45–4.71).

The assessed chemical is highly volatile (vapour pressure = 330 Pa at 20˚C). A large proportion of the assessed chemical is expected to partition to air during STP processing based on SimpleTreat 3.0 model outputs (Struijs 1996). Additionally, when the assessed chemical is released to air it is not expected to partition to other compartments.

Degradation

Based on biodegradation results in water, the assessed chemical is not persistent.

Degradation studies in water indicate that the assessed chemical is readily biodegradable. The result of a biodegradation study supplied for the assessed chemical was 61% degradation (OECD 310) over 28 days.

Bioaccumulation

Based on its high log K_{OW} value, the assessed chemical has potential to bioaccumulate.

No bioaccumulation information was provided for the assessed chemical. The experimental partition coefficient of the assessed chemical has a range of log K_{OW} = 4.45–4.71, which is above the domestic bioaccumulation threshold of log K_{OW} = 4.2 (EPHC 2009). This determination is considered to be conservative as the assessed chemical it not considered to be persistent.

Predicted environmental concentration (PEC)

A predicted environmental concentration (PEC) for Australian waters was calculated assuming 100% of the introduction volume is released into sewage treatment plants (STPs). This calculated value is conservative as not all uses of the assessed chemical are expected to result in release to STPs. Based on its very high vapour pressure, a large proportion of the assessed chemical is expected to partition to air during sewage treatment. Additionally, as the assessed chemical has a high log K_{OW} and is readily biodegradable, it is also expected to be removed through biodegradation and adsorption to biosolids during STP processing. As a result, only a small proportion of the assessed chemical is expected to be present in STP effluent. 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 96%. Therefore 4% 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	96%	Mitigation
Daily effluent production	4,877	ML/day
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10	
PEC - River	0.02	µg/L
PEC - Ocean	0.002	µg/L

Environmental effects

Effects on Aquatic Life

Acute toxicity

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

Taxon	Endpoint	Method
Invertebrate	48 h EL50 = 0.55 mg/L	*Daphnia magna* (Water flea) Immobility OECD TG 202 Semi-static conditions Nominal loading rate
Algae	72 h ErL50 = 38.92 mg/L	*Pseudokircheriella subcapitata* (Green algae) Growth rate OECD TG 201 Static conditions Nominal loading rate

Chronic toxicity

The following measured no-observed-effect loading rates (NOEL) values for model organisms were supplied by the applicant:

Taxon	Endpoint	Method
Algae	72 h NOErL = 1 mg/L	*Pseudokircheriella subcapitata* (Green algae) OECD TG 201 Static conditions Nominal concentration

Predicted no-effect concentration (PNEC)

A predicted no-effect concentration (PNEC) of 1.1 µg/L was calculated for the assessed chemical in the aquatic environment. This value was derived using the most conservative endpoint value for aquatic invertebrates (0.55 mg/L). An assessment factor of 500 was applied to this endpoint as acute toxicity data was only provided for two trophic levels and chronic toxicity data was incomplete (EPHC 2009). The acute endpoint was selected, over the algal chronic endpoint, in the absence of additional chronic endpoints to support the algal growth rate NOErL value and as it is more protective (ECHA 2008).

Categorisation of environmental hazard

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 a measured degradation study, the assessed chemical is categorised as Not Persistent.

Bioaccumulation

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

Toxicity

Toxic (T). Based on available acute ecotoxicity values below 1 mg/L, the assessed chemical is categorised as Toxic.

Environmental risk characterisation

Although the assessed chemical has the potential to bioaccumulate and is toxic, it does not meet all three PBT criteria 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, soil, and sediment:

Compartment	PEC	PNEC	RQ
River	0.02 µg/L	1.1 µg/L	0.02
Ocean	0.002 µg/L	1.1 µg/L	<0.01

For water 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 the levels that are likely to cause harmful effects.

References

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