Australian Government
Department of Health
Australian Industrial Chemicals Introduction Scheme

Terpenes and terpenoids, sinpine

Evaluation statement

14 January 2022

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AICIS evaluation statement

Subject of the evaluation

Terpenes and terpenoids, sinpine

Chemical in this evaluation

Name	CAS number
Terpenes and terpenoids, sinpine	68917-63-5

Reason for the evaluation

The Evaluation Selection Analysis indicated a potential risk to human health.

Parameters of evaluation

The chemical is listed on the Australian Inventory of Industrial Chemicals (the Inventory).This evaluation is a human health risk assessment for all identified industrial uses of the chemical.

Summary of evaluation

Summary of introduction, use and end use

There is currently no specific information about the introduction, use and end use of the chemical in Australia. Based on international use information, the chemical is expected to be used as a fragrance and perfuming agent in cosmetics and personal care products. The chemical is also expected to be used in domestic products, including air fragrance products, polishes, waxes, and in washing and cleaning products.

Human health

Summary of health hazards

Based on the available information for this chemical and the constituent chemicals (γ-terpinene, terpinolene, limonene, and α-pinene), the critical health effects for risk characterisation include the potential of the chemical to cause skin irritation and skin sensitisation.

The chemical is reported to cause moderate skin irritation in a guinea pig study.

The chemical may cause sensory irritation; however, potency would be dependent on the relative proportions of the constituents.

The chemical is considered to be a skin sensitiser based on the positive results seen in adjuvant guinea pig study, in silico data and data for the constituent chemicals. The chemical

is expected to undergo autoxidation to form sensitising hydroperoxides or epoxides, following exposure to air or light.

The chemical may cause an aspiration hazard. This would be dependent on the viscosity of the chemical as introduced. The threshold kinematic viscosity value for classification as an aspiration hazard is 20.5 mm^2/s at 40°C.

Based on the available data for this chemical and the constituents the chemical is:

- expected to have low acute oral and dermal toxicity
- not expected to cause serious damage to health from repeated exposure
- not expected to be genotoxic
- not likely to be carcinogenic
- not considered to cause adverse effect on fertility or development.

Health hazard classification

The chemical satisfies the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (UNECE) for hazard classes relevant for work health and safety as follows. This does not consider classification of physical hazards and environmental hazards.

Health hazards	Hazard category	Hazard statement
Aspiration hazard	Asp Tox. 1	H304: May be fatal if swallowed and enters airways
Skin corrosion/irritation	Skin Irrit. 2	H315: Causes skin irritation
Sensitisation (skin)	Skin Sens. 1	H317: May cause an allergic skin reaction

Summary of health risk

Public

Based on the available use information, the public may be exposed to the chemical by:

- direct application of the chemical to the body during use of cosmetic and personal care products
- incidental skin and eye contact with the chemical during use of domestic products
- inhaling aerosols/vapours during use of cosmetic/domestic products.

Consumer products containing the chemicals can oxidise over time. The auto-oxidation is expected to be limited by the presence of anti-oxidant additives. In Europe, the chemical is restricted in cosmetics and can only be used if the peroxide levels are below 10mM (CosIng). The concentration of the chemical in domestic and cosmetic products is expected to be low, hence peroxide levels are expected to be very low.

Therefore, there are no identified risks to the public that require management.

Workers

During product formulation and packaging, dermal, ocular and inhalation exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed. Good hygiene practices to minimise incidental oral exposure are expected to be in place.

Given the critical local effects the chemical could pose a risk to workers. Control measures to minimise dermal and inhalation exposure are needed to manage the risk to workers (refer to **Recommendation** section).

Conclusions

The conclusions of this evaluation are based on the information described in this statement. Obligations to report additional information about hazards under section 100 of the Industrial Chemicals Act 2019 apply.

The Executive Director is satisfied that the identified human health 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. The proposed means of managing the risks identified during this evaluation are set out in the **Recommendations** section.

Recommendations

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.

The recommended classification and labelling entry should have the following note appended. 'Note 9: The aspiration hazard classification should only be applied if the kinematic viscosity criteria for aspiration classification in the GHS is met'

Information on managing identified risks

The information in this report, including recommended hazard classifications, should be used by persons conducting a business or undertaking (PCBU) at workplace (such as an employer) to determine the appropriate controls under the Model Work Health and Safety Regulations.

Control measures that could be implemented to manage the risk arising from occupational exposure to the chemicals include, but are not limited to:

- using local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker

- minimising manual processes and work tasks through automating processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Measures required to eliminate, or manage risks arising from storing, handling and using a hazardous chemical depend on the physical form and how the chemical is used.

These control measures may need to be supplemented with:

- conducting health monitoring for any worker who is at significant risk of exposure to these chemicals, if valid techniques are available to monitor the effect on the worker's health.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

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.

Supporting information

Rationale

Terpenes and terpenoids, sinpine (CAS No. 68917-63-5) is a UVCB (unknown or variable composition, complex reaction products or of biological materials) chemical. The major constituent chemicals that comprise the UVCB are listed below (REACH), and have been previously assessed under our former scheme, the National Industrial Chemicals Notification and Assessment Scheme, as indicated. The findings from these assessments will be used to provide information on the toxicokinetics, toxicological endpoints of terpenes and terpenoids, sinpine.

- γ-Terpinene [1,4-Cyclohexadiene, 1-methyl-4-(1-methylethyl)-] (CAS No. 99-85-4) (NICNASa 2018)
- Terpinolene [Cyclohexene, 1-methyl-4-(1-methylethylidene)-] (CAS No. 586-62-9) (NICNASa 2018)
- Limonene [1-methyl-4-isopropenyl-1-cyclohexane] (CAS No. 138-86-3) (NICNAS 2002)
- α-Pinene [Bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl-] (CAS No. 80-56-8) (NICNAS 2020)

Chemical identity

Chemical name	Terpenes and terpenoids, sinpine
CAS No.	68917-63-5
Synonyms	dipentene prime sinpine P sinpine redistilled terpenes and terpenoids
Structural formula	No structure available
Molecular formula	Unspecified
Molecular weight (g/mol)	Unspecified
SMILES	Unspecified
Chemical description	The chemical is a UVCB predominantly comprised of γ-terpinene, terpinolene, limonene, and α-pinene.

Relevant physical and chemical properties

Physical form	Liquid (at 20°C and 1013 hPa); pale yellow to yellow; pine-like, fresh aroma; organic.
Melting point	-80°C (at 100.8 kPa)
Boiling point	159–174°C (at 100.8 kPa)
Vapour pressure	0.24–0.4 kPa (at 20–25°C)
Water solubility	12.6–1580 mg/mL (at 19.9–20°C and pH 6.3–6.6)
log K_{ow}	3.1–5.7 (at 35°C and pH 7)

Introduction and use

Australia

No specific Australian use, import, or manufacturing information has been identified for terpenes and terpenoids, sinpine.

International

The following international uses of terpenes and terpenoids, sinpine have been identified (EC; REACH).

The chemical has reported uses in cosmetics and personal care products as a perfuming agent.

The chemical has reported domestic uses, including in:

- air fragrance products
- polishes and waxes
  washing and cleaning products.

The chemical may have commercial and site limited uses as a fragrance or perfuming agent in other products.

Existing Australian regulatory controls

AICIS

No specific controls are currently applicable to the chemical.

Public

No specific restrictions have been identified.

Constituent chemical α-pinene is a major constituent of turpentine oil (NICNASb 2018), which is listed in the Poisons Standard–the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) in Schedule 5 (TGA 2021). Constituent chemicals terpinolene and limonene are also constituents of turpentine oil.

Schedule 5: 'TURPENTINE OIL except in preparations containing 25 per cent or less of turpentine oil.'

Schedule 5 chemicals are described as 'Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label' (TGA 2021).

Workers

The chemical is not listed as hazardous chemicals on the Hazardous Chemicals Information system (HCIS) and no specific exposure standards are available for the chemical in Australia (Safe Work Australia).

International regulatory status

European Union

EU Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products - Annex III - List of Substances which cosmetic products must not contain except subject to the restrictions laid down (ECHA):

Restriction: Peroxide value less than 10 mmoles/L.

New Zealand

New Zealand Cosmetic Products Group Standard - Schedule 5 - Table 1: Components Cosmetic Products Must Not Contain Except Subject to the Restrictions and Conditions Laid Down.

Health hazard information

Toxicokinetics

No specific toxicokinetic data were available for the chemical.

The constituent chemicals terpinolene and γ-terpinene are expected to be bioavailable by the oral and dermal routes. These chemicals may rapidly degrade and form oxidation products following skin contact or exposure to air or light (NICNAS2018).

The constituent chemical limonene is expected to be bioavailable by oral, dermal and inhalation routes. The chemical is rapidly distributed to different tissues in the body including

the brain, adipose tissue, liver, kidney and blood. The chemical is readily metabolised and eliminated primarily through the urine. The chemical undergoes autoxidation following exposure to air or light (NICNAS 2002).

The constituent chemical α-pinene is expected to be bioavailable by oral, dermal and inhalation routes. The chemical is readily metabolised and eliminated (NICNAS 2020).

Acute toxicity

Oral

Based on the available information, the chemical does not warrant hazard classification.

In an acute oral toxicity study, Charles River strain rats (5/sex/dose) were administered the chemical at 1, 2 or 5 mL/kg body weight (bw) in feed. One death was reported in the 5 mL/kg bw group. No further details were available (REACH).

Constituent chemical α-pinene is reported to have moderate acute oral toxicity (NICNAS 2020), and is classified as 'Acute toxicity (oral) - Category 4; Harmful if swallowed (H302)' (SWA).

Constituent chemicals γ-terpinene, terpinolene and limonene are reported to have low acute oral toxicity (NICNASa 2018; NICNAS 2002).

Constituent chemicals γ-terpinene, terpinolene, and α-pinene have the potential to cause an aspiration hazard and are classified as 'Aspiration Hazard – Category 1; May be fatal if swallowed and enters airways (H304) (SWA)'. This is dependent on the viscosity of the chemicals as introduced (NICNASa 2018; NICNAS 2020).

Dermal

No data are available for the chemical. Based on the available information for constituent chemicals, no hazard classification is warranted.

Constituent chemicals γ-terpinene, terpinolene, limonene, and α-pinene are reported to have low acute dermal toxicity (NICNASa 2018; NICNAS 2002; NICNAS 2020).

Inhalation

No data are available for the chemical and limited data are available for constituent chemicals (NICNASa 2018; NICNAS 2002; NICNAS 2020).

Corrosion/Irritation

Skin irritation

Based on the available data, the chemical is expected to be irritating to the skin, warranting hazard classification (see **Recommendation** section).

Application of the chemical (3, 10, 30 or 100% in ethanol) to the clipped skin of guinea pigs (6–8 per group) was reported to cause moderate irritation. No further information was available (REACH).

Constituent chemicals limonene and α-pinene are reported to be skin irritants (NICNAS 2002; NICNAS 2020) and are classified as 'Skin irritation – Category 2; Causes skin irritation (H315) (SWA)'.

Constituent chemicals γ-terpinene and terpinolene are reported to be potentially irritating to the skin but do not meet criteria for hazard classification for skin corrosion/irritation (NICNASa 2018).

Eye irritation

Based on the available data, the chemical is not considered likely to cause eye damage or irritation. No hazard classification is warranted.

In a GLP-compliant ex vivo eye corrosivity/irritation study conducted according to OECD TG 437, the chemical was applied to 3 bovine corneae per experiment. The mean in vitro irritancy score (IVIS) was -0.6 (IVIS >55 is regarded as serious eye damage and IVIS ≤3 is UN GHS No Category). Based on the criteria of the assay, the chemical was not considered to be corrosive or a severe eye irritant.

Constituent chemicals γ-terpinene, terpinolene and limonene are reported to have the potential to cause eye irritation, but with insufficient data to support classification (NICNASa 2018a; NICNAS 2002). Constituent chemical α-pinene is not expected to cause eye irritation (NICNAS 2020).

Respiratory irritation

Based on the available data for limonene and turpentine oil (contains some of the constituents of the chemical) the chemical may cause sensory irritation (NICNASa 2018; NICNASb 2018). The irritation potential would be dependent on the relative proportions of the individual constituents. Sensory irritation is the result of the chemical stimulating the trigeminal nerve endings in the cornea and nasal mucosa, which evokes a stinging or burning sensation in the eyes and upper respiratory tract. This is a receptor mediated mode of action and occurs at relatively low concentrations. Sensory irritation is different to eye and skin irritation used for hazard classification and also does not involve cytotoxicity.

Sensitisation

Skin sensitisation

Based on the available animal and in silico data, the chemical is considered to be a skin sensitiser, warranting hazard classification (see **Recommendation** section).

In an in vivo skin sensitisation study similar to EU Method B.6 (Skin Sensitisation), ≥19 guinea pigs per dose were administered the chemical at 5% by intradermal injection at 0, 4, and 9 days (REACH). Animals also received Freund's Complete Adjuvant. The animals were challenged with the chemical at 1, 3 and 10% at 3 and 5 weeks after the first injection. At 3 weeks, 4/20, 8/20 and 12/20 animals had positive responses to the chemical following challenge at 1, 3 and 10%, respectively. At 5 weeks, 5/19, 7/19 and 13/19 animals had positive responses following challenge at 1, 3 and 10%, respectively. On the basis of these results, the chemical is considered to be a skin sensitiser.

Constituent chemicals terpinolene α-pinene are reported to be skin sensitisers (NICNASa 2018; NICNAS 2020), and are classified as 'Skin sensitisation – Category 1B; May cause an

allergic skin reaction (H317)' (SWA). Constituent chemical limonene is reported to be a skin sensitiser (NICNAS 2002), and is classified as 'Skin sensitisation – Category 1; May cause an allergic skin reaction (H317)' (SWA). The constituent chemicals in their original form (non-oxidised chemical) are not expected to be skin sensitisers. However, the chemicals can form sensitising hydroperoxides or epoxides in contact with oxygen, light or skin (see **In silico data**).

In silico data

No structural alerts for skin sensitisation were present for the constituents alpha-pinene, γ-terpinene, terpinolene or limonene using OECD QSAR Toolbox v4.2. However, when auto-oxidation was simulated there were mechanistic alerts for protein binding.

Respiratory sensitisation

No data were available for the chemical.

Constituent chemicals limonene and α-pinene are reported not to be respiratory sensitisers (NICNAS 2002; NICNAS 2020).

Repeat dose toxicity

Oral

No data were available for the chemical.

Constituent chemicals γ-terpinene, terpinolene and limonene were reported not to cause severe repeated dose toxicity via the oral route.

Repeated dose toxicity studies conducted in rats indicate that terpinolene caused reduced body weight gain which was considered to be secondary to reduced food intake (NICNASa 2018). Increased liver weight was observed, which was considered to be an adaptive response (NICNASa 2018). Renal tubule degeneration was also observed and was noted to be of minimal relevance to humans (NICNASa 2018).

Dermal

No data are available for the chemical or its constituents.

Inhalation

No data are available for the chemical. Based on the weight of evidence, no hazard classification is warranted.

Constituent chemical α-pinene was reported to cause repeated dose toxicity via the inhalation route (NICNAS 2020) and is classified as 'Specific target organ toxicity (repeated exposure) – Category 2; May cause damage to organs through prolonged or repeated exposure (H373)' (SWA). The other constituent chemicals are not classified for repeated dose inhalation toxicity.

Genotoxicity

Based on the available data, the chemical is not considered to be genotoxic.

Negative results were reported in bacterial reverse mutation assays, conducted according to OECD TG 471 in *Salmonella typhimurium* TA 98, 100, 102, 1535 and 1537, with and without metabolic activation, at concentrations up to 5000 µg/plate.

Constituent chemicals γ-terpinene, terpinolene, limonene and α-pinene are reported not to be genotoxic (NICNASa 2018; NICNAS 2002; NICNAS 2020).

Carcinogenicity

No data are available for the chemical.

Constituent chemical limonene is reported not to be carcinogenic (NICNAS 2002).

Reproductive and development toxicity

No data are available for the chemical.

Constituent chemicals γ-terpinene, terpinolene, limonene and α-pinene are reported not to cause reproductive or developmental toxicity (NICNASa 2018; NICNAS 2002; NICNAS 2020).

References

Chemwatch (n.d.) *Galleria Chemica*, Chemwatch website, accessed October 2021.

EC (European Commission) (n.d.) *CosIng*, EC website, accessed October 2021.

ECHA (European Chemicals Agency) (n.d.), *Cosmetic Products Regulation, Annex III - Restricted Substances*, ECHA website, accessed October 2021.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2020*)* *Alpha-pinene: Human health tier II assessment*, NICNAS, accessed October 2021.

NICNASa (National Industrial Chemicals Notification and Assessment Scheme) (2018) *Terpinene, terpinolene and phellandrene: Human health tier II assessment*, NICNAS, accessed October 2021.

NICNASb (National Industrial Chemicals Notification and Assessment Scheme) (2018) *Turpentine: Human health tier II assessment*, NICNAS, accessed October 2021.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2002) *Priority Existing Chemical No. 22*, NICNAS, accessed October 2021.

OECD (Organisation for Economic Co-operation and Development) (2018) *Quantitative Structure-Activity Relationship Toolbox (Version 4.2)*, Computer software, OECD, accessed October 2021.

REACH (n.d.) *Registered dossier for CAS No. 68917-63-5*, European Chemicals Agency website, accessed October 2021.

SWA (Safe Work Australia) (n.d.) *Hazardous Chemical Information System*, SWA website, accessed October 2021.

TGA (Therapeutic Goods Administration) (2021) *SUSMP No.34 (Poisons Standard October 2021)*, TGA, accessed October 2021.

UNECE (United Nations Economic Commission for Europe) (2017) *Globally Harmonized System of Classification and Labelling of Chemicals (GHS) Seventh Revised Edition*, UNECE, accessed October 2021.