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

Cyclopentanol, 2-methyl-5-(1-methylethyl)-, 1-propanoate

Assessment statement (CA09715)

07 February 2024

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AICIS assessment (CA09715)

Chemical in this assessment

Name	CAS registry number
Cyclopentanol, 2-methyl-5-(1-methylethyl)-, 1-propanoate	1245725-35-2

Reason for the assessment

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

Certificate Application type

AICIS received the application in a Very Low to Low Risk type.

Defined scope of assessment

The chemical has been assessed:

- as imported into Australia at up to 1 tonne/year
- as imported in fragrance formulations at up to 1% concentration for local reformulation into finished cosmetic and household products
- as imported or reformulated as a component of finished cosmetic and households products at up to:
    - 0.01% concentration in leave-on and rinse-off cosmetic products (including non-spray deodorants), hair dye, washing and cleaning household products, polishes and wax blends, and air fresheners (instant action)
    - 0.1% concentration in fine fragrances
    - 0.3% concentration in air fresheners (continuous action)

Summary of assessment

Summary of introduction, use and end use

The assessed chemical will not be manufactured in Australia. The assessed chemical will be imported either at up to 1% concentration for further local reformulation into finished cosmetic and household products, or as a fragrance component in finished end use cosmetic and household products and fine fragrances. The cosmetic and household end use products containing the assessed chemical are proposed to be used by professional workers under industrial or non-industrial settings and by members of the general public.

The end use concentration of the assessed chemical for consumer and professional uses will be up to 0.01% in leave-on and rinse-off cosmetic products (including non-spray deodorants), hair dye, washing and cleaning household products, polishes and wax blends and up to 0.1% concentration in fine fragrances. The air fresheners will contain up to 0.01% (instant action) or 0.3% (continuous action) concentration of the assessed chemical.

Human health

Summary of health hazards

The submitted toxicological data on the assessed chemical (see **Supporting information)** indicate that the assessed chemical is:

- of low acute oral toxicity
- slightly irritating to skin and eyes
- not a skin sensitiser
- not expected to cause point mutations

No data on inhalation toxicity or repeated dose toxicity were provided for the assessed chemical.

Hazard classifications relevant for worker health and safety

Based on the data provided by the applicant, 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 adopted for industrial chemicals in Australia.

Physical hazard	Hazard category	Hazard statement
Flammable liquid*	Flam Liq Cat 4	H227: Combustible liquid

* Classified based on measured flash point at 88 °C (see **Supporting information** section)

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 0.3% 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 from the use of air care products and other products applied by spray.

The assessed chemical is slightly irritating to skin and eyes. However, these effects are not expected to occur from the use of the assessed chemical at the proposed low end use concentrations in cosmetics (up to 0.1%). The air fresheners are not expected to cause direct skin or eye contact due to the design of these products.

No inhalation toxicity data were provided for the assessed chemical. Due to the low concentrations of the assessed chemical in end use products, it is not expected to pose a health risk through inhalation when the assessed chemical is used according to the assessed use scenarios.

Considering the low end use concentrations in various products and the toxicological profile of the assessed chemical, the exposure level to the assessed chemical is not expected to pose a health risk to the public through normal use of cosmetic and household products.

Overall, this assessment does not identify any risks to public health that would require specific risk management measures.

Workers

Reformulation workers may be incidentally exposed to the assessed chemical at up to 1% concentration during reformulation processes, mainly via the dermal route, while ocular and inhalation exposures are also possible. To mitigate the risks to reformulation workers from repeated exposure to the assessed chemical, control measures would be required to minimise the exposure (see **Means for managing risk** section). It is anticipated by the applicant that engineering controls such as enclosed and automated processes and local ventilation will be implemented where possible. According to the applicant, use of appropriate personal protective equipment (PPE) such as safety glasses, impervious chemical resistant gloves, protective clothing and respiratory protection will further reduce worker exposure.

Professional workers in cleaning or cosmetic businesses may experience exposure via dermal, inhalation or accidental ocular exposure to the assessed chemical during the use of cleaning or cosmetic products containing the assessed chemical at up to 0.3% concentration. The professional workers may wear PPE (including gloves, safety glasses or face masks, and coveralls). If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using the same end use products containing the assessed chemical, requiring no specific risk management measures for these workers.

Environment

Summary of environmental hazard characteristics

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

- Not Persistent (Not P)
- Bioaccumulative (B)
- Not Toxic (Not T)

Environmental hazard classification

The assessed chemical satisfies the criteria for classification according to the GHS (UNECE 2017) as Acute Category 2 (H401) and Chronic Category 2 (H411) based on the toxicity data for aquatic invertebrates. Considerations were also made for the biodegradation and bioaccumulation of the assessed chemical:

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (acute / short-term)	Aquatic Acute 2	H401: Toxic to aquatic life
Hazardous to the aquatic environment (long-term)	Aquatic Chronic 2	H411: Toxic to aquatic life with long lasting effects

Summary of environmental risk

The assessed chemical will be introduced as a fragrance ingredient for use in a variety of products. These uses may result in the release of the assessed chemical to sewers and to air.

The assessed chemical is not readily degradable, but it is not persistent based on > 60% degradation in 60 days. The assessed chemical has a potential for bioaccumulation. The assessed chemical is not expected to cause toxic effects in aquatic organisms.

As the assessed chemical does not meet all three PBT criteria, it is unlikely to have unpredictable long-term effects and its risk may be estimated by the risk quotient method (RQ = PEC ÷ PNEC). Based on the expected RQ values < 1 for the river and ocean compartments, 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 classifications relevant to work health and safety (see **Hazard classifications relevant for worker health and safety**).

Information relating to safe introduction and use

The information in this statement, including recommended hazard classifications, should be used by a person conducting a business or undertaking 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 risk arising from exposure to the assessed chemical during reformulation:

- Use of engineering controls such as
  - Enclosed and automated systems where possible
  - Adequate workplace ventilation to avoid accumulation of dusts, mists or aerosols

- Use of safe work practices to
  - Avoid contact with skin and eyes
  - Avoid inhalation of mists or aerosols

- Use of personal protective equipment (PPE)
  - Impervious gloves
  - Protective clothing
  - Respiratory protection where local ventilation may be inadequate

- A copy of the Safety Data Sheet (SDS) should be easily accessible to workers.

Conclusions

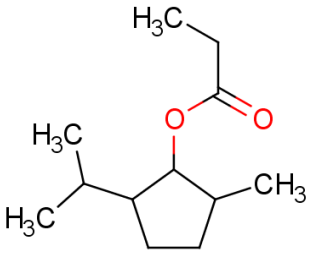
The Executive Director is satisfied that the risks to human health and the environment associated with the introduction and use of the industrial chemical can be managed.

Note:

1. Obligations to report additional information about hazards under s 100 of the *Industrial Chemicals Act 2019* apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Chemical identity

Chemical name	Cyclopentanol, 2-methyl-5-(1-methylethyl)-, 1-propanoate
CAS No.	1245725-35-2
Molecular formula	$C_{12}H_{22}O_2$
Molecular weight (g/mol)	198.30
SMILES (canonical)	O=C(OC1C(C)CCC1C(C)C)CC
Representative structure	

Chemical description

The assessed chemical contains all eight possible stereoisomers with a combined purity between 95% and 100%.

Relevant physical and chemical properties

Physical form	Colourless liquid
Melting point	-114.8 °C
Boiling point	224.3 °C
Vapour pressure	≤ 20.8 Pa at 25 °C
Water solubility	16.3 mg/L at 20 °C
Ionisable in the environment?	No
log K_{ow}	4.26 at 20 °C
log K_{oc}	2.72 – 3.24 (calc.)
Flash point	88 °C
Auto-ignition temperature	263 °C

Health hazard information

Acute toxicity

Oral

In an acute oral toxicity study (OECD TG 423), 6 female Sprague Dawley (SD) rats were administered a single dose of the assessed chemical at 2,000 mg/kg bw. The animals were observed for 14 days after administration. No mortalities, test substance-related clinical signs or macroscopic findings were observed in any of the treated animals and bodyweight gain was normal. Based on the results of this study, the median lethal oral dose (LD50) was determined to be greater than 2,000 mg/kg bw.

Corrosion/Irritation

Skin irritation

In a dermal irritation study (OECD TG 404), a single dose of the assessed chemical was topically applied (semi-occlusive for 4-hours) to the intact skin of three young adult New Zealand White rabbits. A well-defined erythema, associated with a very slight to slight oedema, was noted on the treated area of all animals 24 hours after treatment. The erythema was reversible between days 2 and 7 and the oedema was reversible between days 2 and 5. A slight dryness of the skin was noted from day 2, day 4 or day 5 and was totally reversible by day 13 in one animal and remained on day 14 in the other two animals.

The mean erythema/eschar score of the three animals was 0.7, 1.7 and 1.7, and the mean oedema score was 0.7, 1.7 and 0.7. Therefore, under the conditions of the study, the assessed chemical is considered a slight skin irritant.

Eye irritation

The eye irritation potential of the assessed chemical was investigated in rabbits (OECD TG 405). A volume of 0.1 mL of the assessed chemical was placed into the conjunctival sac of one eye of each of three female New Zealand White rabbits. The ocular reactions observed during the study were slight to moderate and transient in all 3 animals. A moderate redness, noted 1 hour after treatment, had resolved between day 2 and day 4. A slight to moderate chemosis, also noted 1 hour after treatment, had resolved between day 1 and day 2. No corneal or iridial effects were observed at any time point during the study. Mean individual scores for the 3 animals were 1.0, 0.3 and 1.0 for conjunctivae and 0.3, 0.0 and 0.3 for chemosis. Therefore, under the conditions of the study, the assessed chemical is considered slightly irritating to the eyes.

Sensitisation

Skin sensitisation

The skin sensitisation potential of the assessed chemical was tested using a modified local lymph node assay (LLNA) in mice (OECD TG 429). Three groups of four female mice (CBA/J) received topical application of 25 µL of the assessed chemical at concentrations of 25%, 50% or 100% (in acetone/olive oil 4:1) to the dorsal surface of each ear for 3 consecutive days. A control group of four female mice was treated with the vehicle (acetone:olive oil, 4:1) only. Similar to the first experiment, a second experiment was also conducted at 5% and 10%

concentration of the assessed chemical to determine the EC1.4 value. On day 6 (end of the study), the draining auricular lymph nodes from the four mice were excised, pooled for each experimental group, and a single cell preparation carried out for calculation of proliferation responses.

There were no signs of systemic toxicity and body weights were comparable to controls. The stimulation index (SI) at 25%, 50% and 100% concentrations were 1.84, 1.87 and 2.45, respectively. The SI at 5% and 10% concentrations were 0.95 and 1.21, respectively. Based on these results, the EC1.4 value (1.4-fold increase in lymphocyte cell number) was calculated (by linear interpolation) to be 14.5%. It is noted that, based on the EC1.4 value of 14.5%, the authors of the study classified the assessed chemical as a skin sensitiser. However, the GHS 7 states that "For category 1, a stimulation index of three or more is considered a positive response in the local lymph node assay".

Therefore, the assessed chemical does not satisfy the criteria for classification as a skin sensitiser according to the GHS (UNECE 2017).

Genotoxicity

A study was performed to evaluate the potential of the assessed chemical to cause point mutations in a bacterial reverse mutation assay using *Salmonella typhimurium* strains (TA98, TA100, TA1535, TA1537) and *Escherichia coli* strain WP2uvrA (pKM101), in both the presence and absence of metabolic activation (S9-mix) (OECD TG 471). No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, with any tested dose of the assessed chemical, either with or without metabolic activation (S9-mix). Under the conditions of this study, the assessed chemical was not considered to be mutagenic either in the presence or absence of metabolic activation.

No other genotoxicity data were provided.

Environmental exposure

The assessed chemical will be imported into Australia for use as a fragrance in end use products, or as a component of fragrance formulations for reformulation into end use products. Reformulation and repackaging will occur in both closed and open processes. Significant releases of the assessed chemical to the environment are not expected during reformulation, transport or storage.

The assessed chemical will be included in a wide range of products, resulting in a variety of potential exposure scenarios.

Consumer and professional end use of the assessed chemical in polish and wax blends, cosmetic products, washing, cleaning and disinfection 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 partitioning of the assessed chemical was not determined. The chemical is treated as if it is mobile in the environment as a worst-case scenario.

Degradation

Degradation studies in water indicate that the assessed chemical is not readily biodegradable but will not be persistent. A supplied OECD 301D biodegradation study for the assessed chemical demonstrated 37% and 66% degradation of the assessed chemical over 28 days and 60 days, respectively. Therefore, the assessed chemical is categorised as not persistent based on > 60% degradation in 60 days.

Bioaccumulation

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

No bioaccumulation information was provided for the assessed chemical. The experimental partition coefficient of the assessed chemical (log K_{OW} = 4.26) is above the domestic bioaccumulation threshold of log K_{OW} = 4.2 (EPHC 2009).

Predicted environmental concentration (PEC)

A predicted environmental concentration (PEC) for Australian waters was calculated assuming the maximum allowable introduction volume for environmental exposure band 2 (1,000 kg/year) with a release reduction factor of 1 for down-the-drain style end use scenarios. Correspondingly, 100% of the introduction volume is released into sewage treatment plants (STP) over 365 days per year. The extent to which the assessed chemical is removed from the effluent in STP processes was not calculated as a worst-case scenario.

This calculated value is conservative as not all uses of the assessed chemical are expected to result in release to STP.

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	L/person/day
Population of Australia	25.423	Million
Removal within STP	0%	Mitigation
Daily effluent production	5,085	ML/day
Dilution Factor - River	1	
Dilution Factor - Ocean	10	
PEC - River	0.54	µg/L
PEC - Ocean	0.05	µg/L

Environmental effects

Effects on aquatic Life

Acute toxicity

The following measured or calculated median effective concentration (EC50) values for model organisms were supplied by the applicant:

Taxon	Endpoint	Method
Invertebrate	48 h EC50 = 1.99 mg/L	*Daphnia magna* (Water flea) Immobility OECD TG 202 Static conditions Analytically confirmed nominal concentrations
Algae	72 h EC50 = 2.9 mg/L	*Desmodesmus subspicatus* (green algae) Growth rate iSafeRat HA-QSAR v1.9 Ecotox module Calculated concentration

Predicted no-effect concentration (PNEC)

The predicted no-effect concentration is expected to be greater than 0.54 µg/L.

The available standard acute ecotoxicity endpoints for this chemical are greater than 0.54 mg/L. With a conservative assessment factor of 1,000, the lowest calculable PNEC is greater than 0.54 µg/L.

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 high measured log K_{OW} value, the assessed chemical is categorised as Bioaccumulative.

Toxicity

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

Environmental risk characterisation

Although the assessed chemical is bioaccumulative, it does not meet all three PBT criteria. It is hence unlikely to have unpredictable long-term effects (EPHC 2009). An estimate of risk may therefore be determined using the risk quotient method:

Compartment	PEC	PNEC	RQ
River	< 0.54 µg/L	> 0.54 µg/L	< 1
Ocean	< 0.05 µg/L	> 0.54 µg/L	< 0.1

The risk quotient for the aquatic compartment is expected to be less than 1. This is based on a conservative PEC, assuming 100% release of 1 tonne/year to STPs and no removal from the aqueous stream during STP processes, and a conservative PNEC based on an assessment factor of 1,000 and acute aquatic toxicity endpoints for the chemical that each exceed 0.54 mg/L.

Therefore, based on the expected RQ < 1 the assessed chemical is not expected to pose a significant risk to the environment. As such, the environmental risks associated with the assessed chemical can be managed.

References

EPHC (Environment Protection and Heritage Council) (2009), 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.

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