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

Hexanal, 6-cyclopentylidene-

Assessment statement (CA09689)

20 September 2023

Final

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AICIS assessment statement (CA09689)

Chemical in this assessment

Name	CAS registry number
Hexanal, 6-cyclopentylidene-	111998-18-6

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 a fragrance component imported into Australia at up to 1 tonne/year
- as imported in fragrance formulations at up 0.05% concentration for reformulation of end use cosmetics and household products
- as imported or reformulated in continuous action air fresheners at up to 0.05% concentration, in fine fragrances at up to 0.01% concentration, in instant action air fresheners at up to 0.01% concentration, and in other cosmetic and household products at up to 0.01% concentration

Summary of assessment

Summary of introduction, use and end use

The assessed chemical will not be manufactured in Australia. It will be imported either in fragrance formulations at 0.05% concentration for reformulation into cosmetic and household products, or as a component in formulated end use cosmetic and household products. The end use concentration of the chemical will be up to 0.05% in continuous action air fresheners and 0.01% in instant action air fresheners, fine fragrances and other cosmetic or household products.

The cosmetic and household end use products containing the chemical are proposed to be widely used by the professional workers under industrial or non-industrial settings and by members of the general public.

Human health

Summary of health hazards

The submitted toxicological data on the assessed chemical (see **Supporting information** and **Hazard classifications relevant for worker health and safety** section) indicate that the assessed chemical is:

- of low acute dermal toxicity
- not mutagenic in a bacterial reverse mutation assay

The submitted data also indicate that the assessed chemical:

- is harmful if swallowed
- causes skin irritation
- causes serious eye damage
- is a weak skin sensitiser

No data on inhalation toxicity and repeated dose toxicity data was provided.

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 adopted for industrial chemicals in Australia as follows:

Health hazards	Hazard category	Hazard statement
Acute toxicity oral	Acute tox. 4	H302: Harmful if swallowed
Skin irritation	Skin Irrit. 2	H315: Causes skin irritation
Eye irritation	Eye Irrit. 1	H318: Causes serious eye damage
Skin sensitisation	Skin Sens. 1B	H317: May cause an allergic skin reaction

Summary of health risk

Public

There will be widespread and repeated exposure of the public to the assessed chemical at up to 0.05% concentration from the use of continuous action air-fresheners and 0.01% concentration through the use of a wide range of cosmetic and household products. The principal route of exposure will be dermal and inhalation, while incidental oral or ocular exposure is also possible. Inhalation exposure occurs particularly from the use of air care products and other products applied by spray.

The assessed chemical is irritating to skin, severely irritating to eyes and is a weak skin sensitiser. However, these effects are not expected to occur from use of the assessed chemical at the proposed low end use concentrations (up to 0.01%) in cosmetic and household products

except for continuous action air fresheners (up to 0.05%). The continuous action air fresheners are not expected to come into direct contact with skin or eyes due to designed nature of the products.

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

Furthermore, due to the very low end use concentrations of the assessed chemical in cosmetic and household products the assessed chemical is unlikely to pose health risk to the public through repeated or prolonged exposure if it is used according to the assessed use scenarios.

Overall, this assessment does not identify any risks to public health that would require specific risk management measures if the assessed chemical is introduced and used in accordance with the terms of the assessment certificate.

Workers

Reformulation workers may be incidentally exposed to the assessed chemical at up to 0.05% concentration during reformulation processes mainly via the dermal route, while ocular and inhalation exposure are also possible. However, the assessed chemical will only be introduced at a maximum concentration of 0.05%, at which the chemical is unlikely to pose health risks to workers. It is anticipated by the applicant that the engineering controls such as enclosed and automated processes and local ventilation will be implemented where possible. Use of appropriate personal protective equipment (PPE) such as safety glasses, impervious chemical resistant gloves, protective clothing and respiratory protection will reduce worker exposure.

Professional workers in cleaning or cosmetic businesses may experience exposure via dermal, inhalation and accidental ocular exposure to the assessed chemical during the use of cleaning or cosmetic products containing the assessed chemical at up to 0.05% concentration. The professional workers may wear some PPE (including gloves, coveralls, safety glasses and face masks). 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 chemical is:

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

Environmental hazard classification

The chemical satisfies the criteria for classification according to the GHS (UNECE 2017) as Acute Category 1 (H400) and Chronic Category 1 (H410) based on the toxicity data for aquatic organisms. Considerations were also made for the rapid degradation and bioaccumulation potential of the assessed chemical.

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (acute / short-term)	Aquatic Acute 1	H400: Very toxic to aquatic life
Hazardous to the aquatic environment (long-term)	Aquatic Chronic 1	H410: Very 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 cosmetic and household products. These end uses will result in the release of the assessed chemical to sewers and to air.

The assessed chemical is readily biodegradable and is not persistent. The assessed chemical is not expected to bioaccumulate but is toxic to aquatic organisms.

As the assessed chemical is not bioaccumulative or persistent 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 and use of the assessed chemical can be managed.

Means for managing risk

Workers

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.

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

- No specific engineering controls, work practices or personal protective equipment are required for the safe use of the assessed chemical when it is introduced and used at a maximum concentration of 0.05% and in accordance with the terms of the certificate. However, safety measures should be taken on the basis of all ingredients in the formulations.
- A copy of the Safety Data Sheet (SDS) should be easily accessible to workers.

Conclusions

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

Considering the 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 means for managing the risks identified during this assessment are implemented.

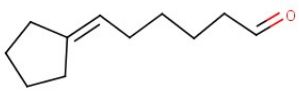
Note: Obligations to report additional information about hazards under section 100 of the *Industrial Chemicals Act 2019* apply.

Supporting information

Chemical identity

Chemical name	Hexanal, 6-cyclopentylidene-
CAS No.	111998-18-6
Synonyms	6-Cyclopentylidenehexanal
Molecular formula	$C_{11}H_{18}O$
Molecular weight (g/mol)	166.26
SMILES (Canonical)	O=CCCCCC=C1CCCC1

Structure



Chemical description

The assessed chemical has a degree of purity between 80% and 100% (w/w).

Relevant physical and chemical properties

All measured values are based on the studies provided on the assessed chemical and conducted according to a reliable test guideline.

Physical form	Clear light-yellow liquid (turning to clear pink liquid over time)
Melting point	Less than -20 °C
Boiling point	248.9 ± 0.2 °C at 101.3 kPa
Relative density (D20/4)	0.93 ± 0.05 at 20 °C
Vapour pressure	0.0073 kPa at 25 °C (QSAR prediction*)
Water solubility	62.1 mg/L at 20 °C
Ionisable in the environment	No
log K_{ow}	4.18 at 20 °C (pH = 7.3)
log K_{oc}	2.09 - 3.01 (calculated)
Flash point	106.0 °C

* Calculated value from iSafeRat® HA-QSAR toolbox v2.5.

Health hazard information

The results from toxicological investigations conducted on the assessed chemical provided by the applicant are summarised in the following table.

Endpoint	Test guideline	Results and Conclusion
Rat, acute oral toxicity	OECD TG 423	LD50 > 300 but < 2,000 mg/kg bw; harmful
Rat, acute dermal toxicity	OECD TG 402	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	OECD TG 404	Irritating
Rabbit, eye irritation	OECD TG 405	Serious eye damage
Skin sensitisation – LLNA	OECD TG 429	Evidence of sensitisation
Mutagenicity – bacterial reverse mutation	OECD TG 471	Non-mutagenic

Acute toxicity

Oral

In an acute oral toxicity study (OECD TG 423), 3 female Sprague Dawley rats were administered the assessed chemical via oral gavage at a single dose of 2,000 mg/kg bw. An additional group of 6 female rats were administered at a dose of 300 mg/kg bw.

At 2,000 mg/kg bw dose, clinical signs of toxicity observed were decreased in spontaneous activities (3/3), piloerection (3/3), bradypnoea (1/3) and total ptosis (1/3). Two rats died approximately 23 hours after the treatment. Significant decrease (between 11 to 15%) in body weight was noted in the 2 rats on the day of the death compared to day 0. Rigor mortis was noted before the necropsy in both rats. In the surviving animal, absence of body weight gain was noted on day 2 but returned to normal during the observation period. Macroscopic examination of the animals that died revealed a thinning of the forestomach associated with black and red spots on the forestomach and on the corpus.

While there were no mortalities at 300 mg/kg bw dose, clinical signs of systemic toxicity noted were decrease in spontaneous activities (3/6) and piloerection (2/6). Both these effects were transient in nature and the animals appeared normal 4 hours post exposure. Expected body weight gains were noted during the observation period.

The median lethal dose (LD50) of the assessed chemical was determined to be higher than 300 mg/kg bw and lower than 2,000 mg/kg bw in rats. Based on the results of this study, the assessed chemical warrants hazard classification for acute oral toxicity (Category 4, H302: Harmful if swallowed) according to GHS criteria.

Dermal

In an acute dermal toxicity study in Sprague Dawley rats (OECD TG 402), the assessed chemical was applied to the intact skin of 10 rats (5 males and 5 females) at a single dose of

2,000 mg/kg bw. No mortality occurred during the study. No systemic clinical signs related to the treatment were observed. Erythema was noted in all animals 24 hours after the treatment. The skin effect was reversible on day 2 in males and on day 8 in females. Dryness of the skin was noted on day 3 in all females and was reversible between days 5 and 8.

The body weight of the animals remained normal throughout the study. The macroscopic examination at the end of the study did not reveal treatment-related changes.

The LD50 of the assessed chemical was determined to be higher than 2,000 mg/kg bw via dermal route in rats. Based on the results of this study, the assessed chemical is of low acute dermal toxicity.

Irritation

Skin irritation

The assessed chemical was determined to be irritating to the skin of rabbits (OECD TG 404).

Well-defined (2/3) or moderate to severe (1/3) erythema and severe oedema (3/3) were observed 1 hour after treatment. All signs of irritation were resolved after 72 hours (2/3) and 7 days (1/3). Skin dryness was observed in 72 hours to day 7 after the exposure but all animals recovered within 14-day observation period. No mortalities or other clinical signs of toxicity were observed.

Based on the results of this study, the assessed chemical warrants hazard classification for skin irritant (Category 2, H315: Causes skin irritation) according to GHS criteria.

Eye irritation

The assessed chemical was determined to be severely irritating to the eyes in an eye irritation study in rabbits (OECD TG 405).

Starting from 1-hour observation, redness (grade 3) and chemosis (grade 3) were reported in the conjunctiva of the animal at each observation point. The irritation effects were reversible on day 21. Scattered to diffuse corneal opacity (grade 2) was seen along with congestion in the iris 1 hour after the test item instillation. While iris congestion was reversible on day 7, corneal opacity remained at grade 2 at 72-hour observation and then increased to grade 3 from day 7 until the end of the 21-day observation period.

Based on the results of this study, the assessed chemical warrants hazard classification for eye irritation (Category 1, H318: Causes serious eye damage) according to GHS criteria.

Sensitisation

Skin sensitisation

In a mouse local lymph node assay (OECD 429), no mortalities and signs of systemic toxicity were noted during the study. No significant increase in ear thickness and ear weight was noted in the test animals. All the animals showed expected body weight gain.

Stimulation indices calculated for 2.5%, 5%, 10%, 25%, 50% and 100% concentrations were 1.24, 1.33, 1.56, 1.72, 2.28, and 3.24 respectively. The concentration of the test substance

expected to result in a 1.4-fold stimulation index (EC1.4 value) was calculated (by linear interpolation) to be 6.25%.

There was evidence of a lymphocyte proliferative response indicative of skin sensitisation to the assessed chemical.

Based on the results of this study, the assessed chemical was determined to be a skin sensitiser and warrants hazard classification for skin sensitisation (Category 1B, H317: May cause an allergic skin reaction) according to GHS criteria.

Genotoxicity

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

Environmental exposure

The assessed chemical will be imported into Australia for use as a fragrance in end use cosmetic and household products, or as a component of fragrance formulations for reformulation into the 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 readily biodegradable and not persistent. Two supplied OECD TG 301D and EU method C.4-E biodegradation studies for the assessed chemical demonstrated 73.5% and 86.56% degradation over 28 and 21 days, respectively. The assessed chemical satisfied the 10-day-window criterion.

Bioaccumulation

No bioaccumulation information was provided for the assessed chemical. The experimental partition coefficient of the assessed chemical (log K_{OW} = 4.18) is below the domestic bioaccumulation threshold of log K_{OW} = 4.2 (EPHC, 2009). Therefore, bioaccumulation of the assessed chemical is not expected.

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/annum) 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 annum. 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 median lethal concentration (LC50) and median effective concentration (EC50) values for model organisms were supplied by the applicant:

Taxon	Endpoint	Method
Fish	96 h LC50 = 5.2 mg/L	*Danio rerio* (Zebra fish) OECD TG 203 Semi-static conditions Geometric mean measured concentration
Invertebrate	48 h EC50 = 0.76 mg/L	*Daphnia magna* (water flea) immobilisation iSafeRat HA-QSAR v1.8 Ecotox module Calculated concentration
Algae	72 h E_rC50 = 2.1 mg/L	*Desmodesmus subspicatus* (Green algae) Growth rate OECD TG 203 Semi-static conditions Geometric mean measured concentration

Chronic toxicity

The following measured no-observed-effect concentration (NOEC) value for a model organism was supplied by the applicant:

Taxon	Endpoint	Method
Algae	72 h NOEC = 0.4 mg/L	*Desmodesmus subspicatus* (Green Algae) Growth rate OECD TG 203 Semi-static conditions Geometric mean measured 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 > 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

Not Bioaccumulative (Not B). Based on low measured log K_{OW} value, the assessed chemical is categorised as Not Bioaccumulative.

Toxicity

Toxic (T). Based on an available ecotoxicity value below 1 mg/L for daphnia, the assessed chemical is categorised as Toxic.

Environmental risk characterisation

The assessed chemical is not persistent or 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/annum 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 (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

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