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

2*H*-Pyran, tetrahydro-3-(phenylmethyl)-

Assessment statement (CA09704)

19 September 2023

Final

Table of contents

AICIS assessment statement (CA09704)

Chemical in this assessment

Name	CAS registry number
2*H*-Pyran, tetrahydro-3-(phenylmethyl)-	60466-73-1

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 to 1% concentration for reformulation of end use cosmetics and household products
- as imported or reformulated in continuous action air fresheners at up to 0.5% concentration, in fine fragrances at up to 0.1% concentration, in instant action air fresheners at up to 0.05% concentration, and in other cosmetic and household products at up to 0.02% 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 up to 1% concentration or in end use cosmetic and household products at various concentrations as shown below:

Product type	Proposed end use concentration (%)
Continuous action air fresheners	0.5
Fine fragrance	0.1
Instant action air fresheners	0.05
Other leave-on and rinse-off cosmetic products	0.02

Product type	Proposed end use concentration (%)
Other household products	0.02

Based on the submission, in addition to liquid reformulations the assessed chemical may also be formulated into solid preparations by tabletting, compression, extrusion or pelletisation. The cosmetic and household end use products containing the chemical are proposed to be used by 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 indicate that the assessed chemical is (see **Supporting Information** and **Health hazard classification** section):

- of low acute oral toxicity
- slightly irritating to skin
- not a skin sensitiser
- not expected to be genotoxic

The submitted data on the chemical also indicate that the assessed chemical is:

- irritating to eyes warranting hazard classification

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

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
Eye irritation	Category 2A	H319: Causes serious eye irritation

Summary of health risk

Public

There will be widespread and repeated exposure of the public to the assessed chemical at up to 0.5% 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 slightly irritating to skin and irritating to eyes. However, irritation effects are not expected to occur from use of the assessed chemical at the proposed low end use concentrations (up to 0.5%) in cosmetic and household products.

No inhalation toxicity data are 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.

No repeated dose toxicity data were provided on the assessed chemical. Based on the proposed very low end use concentrations, cumulative exposure from simultaneously using multiple end use cosmetic and household products containing the assessed chemical (worst case exposure scenario) is not expected to pose systemic health risk to the public through repeated exposure.

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 1% concentration during reformulation processes mainly via the dermal route, while ocular and inhalation exposures are also possible. To mitigate potential repeated dose exposure risks to reformulation workers, control measures would be required (see **Means for managing risk**) to minimise the exposure. It is anticipated by the applicant that 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 0.02% concentration. The professional workers may wear some PPE (including gloves, safety glasses, coveralls 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 available data the chemical is:

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

Environmental hazard classification

The chemical satisfies the criteria for classification according to the GHS (UNECE, 2017) as Acute Category 3 (H402) and Chronic Category 3 (H412) based on the toxicity data for fish. Considerations were also made for the degradation of the assessed chemical.

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (acute / short-term)	Aquatic Acute 3	H402: harmful to aquatic life
Hazardous to the aquatic environment (long-term)	Aquatic Chronic 3	H412: Harmful 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 not readily biodegradable but is inherently biodegradable and is not persistent. The assessed chemical has a low potential for bioaccumulation and is harmful to 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 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

- The following control measures should be implemented to manage the risk arising from exposure to the assessed chemical during reformulation:
    - Use of engineering controls such as
        - automated and enclosed systems where possible

        - adequate workplace ventilation to avoid accumulation of vapours, mists, or aerosols

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

    - Use of personal protective equipment (PPE)
        - overalls
        - gloves
        - respiratory protection if required

- 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.

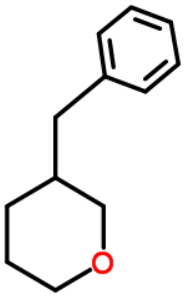
Note: Obligations to report additional information about hazards under section 100 of the *Industrial Chemicals Act 2019* apply.

Supporting information

Chemical identity

Chemical name	2*H*-Pyran, tetrahydro-3-(phenylmethyl)-
CAS No.	60466-73-1
Synonyms	Tetrahydro-3(phenylmethyl)-2*H*-pyran
Molecular formula	$C_{12}H_{16}O$
Molecular weight (g/mol)	176.26
SMILES (Canonical)	O1CCCC(C1)CC=2C=CC=CC2
Purity	> 90 - < 100% (w/w)

Representative Structure:



Chemical description

The assessed chemical is a mixture of two stereoisomers (R and S).

Relevant physical and chemical properties

Physical form	Colourless translucent liquid at room temperature
Melting point	-4.1°C
Boiling point	266.4 °C at 100.8 kPa
Relative density (D20/20)	1.006 at 20 °C
Vapour pressure	0.00346 kPa at 25 °C (QSAR prediction)
Water solubility	442 - 537 mg/L (calculated*)
log K_{ow}	2.97

log K_{oc}	2.49 - 3.09 (calculated)
Flash point	122.0 °C

* Calculated value from iSafeRat® holistic HA-QSAR version 1.8.

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 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	OECD TG 404	Slightly irritating
Rabbit, eye irritation	OECD TG 405	Irritating
Skin sensitisation – Guinea pig maximisation test	OECD TG 406	Non sensitising
Mutagenicity – bacterial reverse mutation	OECD TG 471	Non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration test	OECD TG 473	Non clastogenic

Acute toxicity

Oral

Acute toxicity potential of the assessed chemical was tested following the OECD TG 423. The assessed chemical was administered by oral gavage to Sprague Dawley rats at the single dose of 2,000 mg/kg bw. No mortality occurred during the study and no clinical signs related to the treatment were recorded. The body weight in both treated and control animals remained in the normal range with no statistical significance. The macroscopical examination of the animals at the end of the study did not reveal treatment-related changes. Based on the results of this study, the assessed chemical is of low acute oral toxicity.

Corrosion/Irritation

Skin irritation

Skin irritation potential of the assessed chemical was tested in rabbits following the OECD TG 404. Skin of 3 New Zealand White male rabbits were exposed to the undiluted assessed chemical at the dose of 0.5 mL for 4 hours under semi-occlusive conditions. Slight to moderate erythema (maximum score of 2) was noted in all test animals 24 hours after exposure. Skin dryness was also noted during the study. The erythema effects were reversed within 5 days and the dryness was recovered within 8 days. Based on the results, the assessed chemical is

considered as slightly irritating to the skin but does not meet the GHS criteria for classification as adopted by Australia for industrial chemicals.

Eye irritation

The eye irritation potential of the assessed chemical was tested in rabbits following the OECD TG 405. Eyes of 3 New Zealand White female rabbits were exposed to the undiluted assessed chemical at a dose of 0.1 mL. All 3 test animals exhibited test substance related moderate ocular effects, including conjunctive chemosis and redness (both maximum score of 2), iris lesions (maximum score of 1) and corneal opacity (maximum score of 2), which were reversible in 12 days. Based on the ocular effects observed, the assessed chemical meets the GHS criteria for classification as irritating to eyes (Cat 2A: H319: Causes serious eye irritation).

Sensitisation

Skin sensitisation

A guinea pig maximisation test (GPMT) following Magnusson and Kligman maximisation method (OECD TG 406) was conducted to assess skin sensitisation potential of the assessed chemical. Ten test animals were induced with the assessed chemical (intradermal injection at 25% and topical application at 100% concentrations). After 18 days, the test animals were challenged with 50% and 100% concentrations of the assessed chemical and skin reactions were recorder 24 hours after application. No skin reactions attributable to allergy was observed. The assessed chemical was not a skin sensitiser under the test conditions.

Genotoxicity

Mutagenic potential of the assessed chemical was tested in a bacterial reverse mutation assay following the OECD TG 471 using the plate incorporation and pre-incubation methods. *Salmonella typhimurium* strains TA 1535, TA 1537, TA 98 and TA 100 and *Escherichia coli* strain WP2uvrA- were used for the test. The chemical was tested at up to 1,500 µg/plate in the absence or presence of metabolic activation system (S9 mix). No test substance mediated increase in number of revertant colonies were observed under any test conditions and the chemical was not considered as mutagenic.

An in vitro chromosome aberration test following OECD TG 473 was conducted to assess clastogenic potential of the assessed chemical. The test was conducted using cultured human lymphocytes. The chemical was tested at up to 1,762.6 µg/mL in the absence or presence of metabolic activation system (S9 mix). When tested at up to cytotoxic concentrations, the assessed chemical did not induce any significant increase in the frequency of cells with chromosome aberrations under any test conditions. The chemical was not considered as clastogenic to human lymphocytes in vitro.

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 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

Based on its measured degradation in water, the assessed chemical is categorised as not persistent.

The result of a supplied biodegradation study conducted using the OECD test guideline 301F demonstrated 7% degradation of the assessed chemical in 28 days. The study was prolonged to 49 days to assess any further degradation. The assessed chemical reached 62% degradation in this period. Therefore, the assessed chemical is not considered readily biodegradable, but is not persistent in water.

Bioaccumulation

No bioaccumulation information was provided for the assessed chemical. The experimental partition coefficient of the assessed chemical (log K_{OW} = 2.97) 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 calculated median effective concentration (EC50) values for model organisms were supplied for the assessed chemical:

Taxon	Endpoint	Method
Fish	96 hr LC50 = 20.1 mg/L	*Brachydanio rario* (zebrafish) OECD TG 203 Semi-static conditions Measured concentration
Invertebrate	48 hr EC50 = 19 mg/L	*Daphnia magna* (water flea) immobilisation iSafeRat HA-QSAR v1.8 Ecotox module Calculated concentration
Algae	72 hr ErC50 = 18 mg/L	*Pseudokirchneriella subcapitata* (green algae) Growth rate iSafeRat HA-QSAR v1.8 Ecotox module Calculated concentration

Predicted no-effect concentration (PNEC)

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

As indicated in the 'Effects on aquatic Life' section, 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 measured degradation studies, 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

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

The assessed chemical does not meet any of the PBT criteria. It is hence unlikely to have unpredictable long-term environmental 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.