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

2*H*-Pyran-2-one, tetrahydro-5-propyl-

Assessment statement (CA09703)

25 September 2023

Final

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AICIS assessment (CA09703)

Chemical in this assessment

Name	CAS registry number
2*H*-Pyran-2-one, tetrahydro-5-propyl-	214335-70-3

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 0.55% concentration, in fine fragrances at up to 0.2% concentration, in instant action air fresheners at up to 0.05% concentration, in other cosmetic products at up to 0.02% concentration and in other 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 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	0.55
Fine fragrance	0.2
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	0.01

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 (see **Supporting information** section) indicate that the assessed chemical is:

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

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

Hazard classifications relevant for worker health and safety

Based on the available data, the assessed chemical is not classified according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE 2017), as adopted for industrial chemicals in Australia.

Summary of health risk

Public

There will be widespread and repeated exposure of the public to the assessed chemical at up to 0.55% concentration from the use of air-fresheners and up to 0.02% 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 eyes. However, these effects are not expected to occur from use of the assessed chemical at the proposed low end use concentrations (up to 0.2%) in cosmetic and household products except for continuous action air fresheners (up to 0.55%). 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.

No repeated dose toxicity data were provided on the assessed chemical. Based on the quantitative risk assessment (QRA) for the worst-case scenario, consumers simultaneously using multiple cosmetics and household products may be systemically exposed to the assessed chemical at approximately 63 µg/kg bw/day through repeated or prolonged exposure (see **Supporting information** section). Considering the low systemic exposure level to the assessed chemical health risks from repeated exposure to the public are not expected.

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 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 0.55% 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 the 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: harmful to aquatic life) based on the toxicity data for fish.

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (acute / short-term)	Aquatic Acute 3	H402: harmful to aquatic life

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 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 be bioaccumulative and is not expected to cause toxic effects in aquatic organisms.

As the assessed chemical does not meet any of the 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.

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.

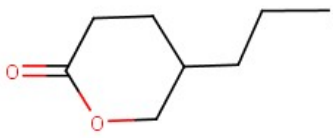
Note: Obligations to report additional information about hazards under section 100 of the *Industrial Chemicals Act 2019* apply.

Supporting information

Chemical identity

Chemical name	2*H*-Pyran-2-one, tetrahydro-5-propyl-
CAS No.	214335-70-3
Synonyms	Tetrahydro-5-propyl-2*H*-pyran-2-one
Molecular formula	$C_8H_{14}O_2$
Molecular weight (g/mol)	142.196
SMILES (Canonical)	O=C1OCC(CC1)CCC
Purity	> 90% (w/w)

Representative Structure



Chemical description

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

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	Colourless translucent liquid
Melting point	-111.4 ± 0.1 ºC
Boiling point	251.7 ± 0.4 °C at 101.3 kPa
Relative density (D20/20)	1.0074 ± 0.0001 at 20 ºC
Vapour pressure	0.0064 kPa at 25 ºC (QSAR prediction[#])
Water solubility	26128 mg/L at 25 ºC (calculated*)
Ionisable in the environment	No
Flash point	137.8 °C

log K_{ow}	1.37
log K_{oc}	1.58 - 1.82 (calculated)

Calculated value from iSafeRat® vapour pressure HA-QSAR v1.3
* Calculated value from iSafeRat® holistic HA-QSAR v1.7.

Human exposure

Public

There will be widespread and repeated exposure of the public to the assessed chemical at up to 0.2% concentration through the use of a range of cosmetic and household products and up to 0.55% concentration when using continuous action air fresheners. The main routes of exposure will be dermal and inhalation, while incidental oral or ocular exposures are also possible.

Dermal exposure

Data on typical use patterns of cosmetic products (SCCS 2012; Cadby et al. 2002; ACI 2010; Loretz et al. 2006) in which the assessed chemical may be used are shown in the following table. A dermal absorption (DA) rate of 100% was used as a worst-case scenario along with a combined average body weight (BW) for males and females of 70 kg (enHealth 2012) for calculation purposes.

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (µg/kg bw/day)
Body lotion	7,820	0.02	1	22
Face cream	1,540	0.02	1	4
Hand cream	2,160	0.02	1	6
Fine fragrances	750	0.2	1	21
Deodorant (non-spray)	1,500	0.02	1	4
Shampoo	10,460	0.02	0.01	0
Conditioner	3,920	0.02	0.01	0
Shower gel	18,670	0.02	0.01	1
Hand wash soap	20,000	0.02	0.01	1
Hair styling products	4,000	0.02	0.1	1
Total				**61**

C = maximum intended concentration of assessed chemical; RF = retention factor
Daily systemic exposure = (Amount × C × RF × DA)/BW

Dermal exposure from using household cleaning products and wearing clothes will result in additional less than 1 µg/kg bw/day systemic exposure, considering low concentrations and retention factors of these products.

Inhalation exposure

Hairspray was taken as a worst-case scenario example for the inhalation exposure assessment. A 2-zone approach was used (Steiling et al. 2014; Rothe et al. 2011; Earnest Jr. 2009). An adult inhalation rate of 20 m^3/day (enHealth 2012) was used and it was conservatively assumed that the fraction of the assessed chemical inhaled is 50%.

Amount of hairspray applied	9.89	g/day
Maximum intended concentration of the chemical	0.02	%
Inhalation rate of the user	20	m^3/day
Exposure duration in zone 1	1	minutes
Exposure duration in zone 2	20	minutes
Fraction inhaled by the user	50	%
Volume of zone 1	1	m^3
Volume of zone 2	10	m^3
Daily systemic exposure	1	µg/kg bw/day

C = maximum intended concentration of assessed chemical
Total daily systemic exposure = Daily systemic exposure in zone 1 [(amount × C × inhalation rate × exposure duration (zone 1) × fraction inhaled)/(volume (zone 1) × body weight)] + Daily systemic exposure in zone 2 [(amount × C × inhalation rate × exposure duration (zone 2) × fraction inhaled)/(volume (zone 2) × body weight)]

It is acknowledged that inhalation exposure to the assessed chemical from use of other cosmetic and household products may also occur.

Overall, the worst-case scenario estimation is for a person who is a simultaneous user of all products listed in the above tables that contain the assessed chemical at the maximum intended concentrations specified in various product types. This would result in a combined internal dose of 63 µg/kg bw/day (= 0.063 mg/kg bw/day) for the assessed chemical. This low level of worst-case systemic exposure is unlikely to pose health risk to the public with repeated use of products containing the assessed chemical.

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	Slightly irritating
Skin sensitisation – Guinea pig maximisation test	OECD TG 406	Not 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

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

No signs of toxicity were observed. All the animals survived, and no abnormalities were observed. The animals showed expected body weight gains throughout the study and did not reveal treatment-related macroscopic changes.

The oral median lethal dose (LD50) of the assessed chemical was determined to be higher than 2,000 mg/kg bw in rats, indicating low acute oral toxicity.

Irritation

Skin irritation

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

A well definite erythema associated with a very slight oedema was noted in all 3 animals 24 hours after the test item application. Very slight (1/3) to well defined erythema (1/3) was noted in all animals at 48 hours after treatment. The oedema effects were reversible between days 3 and 4 and the erythema effects were reversible between days 4 and 7. The skin recovered to normal between the days 5 and 11.

All the animals survived with no clinical signs. Based on the results of this study, the assessed chemical is slightly irritating to the skin but does not warrant a hazard classification under GHS.

Eye irritation

The assessed chemical was determined to be slightly irritating to the eyes of rabbits (OECD TG 405).

Moderate redness (grade 2) associated with moderate chemosis (grade 2) was noted at 1 hour observation in all 3 animals after the test item instillation. The effects were reversible between days 4-6 and days 3-4 of the test, respectively. A moderate opacity (grade 2) was noted at 24 hours after the test item instillation in 2 animals. These effects were reversible between days 3 and 7.

All test animals survived, and no clinical signs were observed. All the animals showed expected body weight gain throughout the study. Based on the study results of this study, the assessed chemical is slightly irritating to the eyes but does not warrant for hazard classification under GHS.

Sensitisation

Skin sensitisation

The assessed chemical was determined to be not sensitising to the skin in a guinea pig maximisation test (GPMT, OECD TG 406). The inductions were conducted using intradermal injections at 3.125% concentration and topical applications at 100% concentration. The test animals were later challenged by topical applications at 50% and 100% concentrations. There was no evidence of skin reactions during the study indicative of sensitisation to the assessed chemical under the conditions of the test.

Genotoxicity

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

The assessed chemical was also found to be non-clastogenic in *an in vitro* mammalian chromosome aberration test using human peripheral blood lymphocytes (OECD TG 473).

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 cosmetic and household products is expected to result in 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 301B test guideline demonstrated 88% degradation of the assessed chemical in 28 days and fulfilled the 10 day window. Therefore, the assessed chemical is considered readily biodegradable.

Bioaccumulation

No bioaccumulation information was provided for the assessed chemical. The measured partition coefficient of the assessed chemical (log K_{OW} = 1.37) 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 calculated 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 = 71 mg/L	*Brachydanio rario* (zebrafish) mortality iSafeRat HA-QSAR v1.8 Ecotox module Calculated concentration
Invertebrate	48 hr EC50 = 175 mg/L	*Daphnia magna* (water flea) immobilisation iSafeRat HA-QSAR v1.8 Ecotox module Calculated concentration
Algae	72 hr ErC50 = 367 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.

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 a measured log K_{OW} value, below the domestic threshold value, the assessed chemical is categorised as Not Bioaccumulative.

Toxicity

Not Toxic (Not T). Based on 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 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	> 0.54µg/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.

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