



Australian Government

Department of Health and Aged Care

Australian Industrial Chemicals Introduction Scheme

2(3*H*)-Furanone, 5-(6-hepten-1-yl)dihydro-, (5*S*)-

Assessment statement (CA09813)

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AICIS assessment (CA09813)

Chemical in this assessment

Name	CAS registry number
2(3H)-Furanone, 5-(6-hepten-1-yl)dihydro-, (5S)-	3017933-60-4

Reason for the assessment/evaluation

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 local reformulation into cosmetics and household products in continuous action air fresheners at up to 0.5% concentration, in fine fragrances and in instant action air fresheners at up to 0.2% concentration, and in other cosmetic and household products at up to 0.02% concentration
- as imported in finished products for sale in continuous action air fresheners at up to 0.5% concentration, in fine fragrances and in instant action air fresheners at up to 0.2% 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 for local reformulation into end use cosmetics and household products or in finished end use cosmetic and household products at various concentrations, including continuous action air fresheners at up to 0.5%, fine fragrances and instant action air fresheners at up to 0.2%, and other cosmetic and household products at up to 0.02% concentrations.

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.

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 and eyes
- not a skin sensitiser
- not mutagenic in a bacterial reverse mutation assay

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

Hazard classifications relevant for worker health and safety

Based on limited data provided by the applicant, the assessed chemical cannot be classified 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.

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 from the use of air fresheners and up to 0.2% 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 are 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, irritation 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. 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 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 a 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 exposure scenario, consumers simultaneously using multiple cosmetic and household products may be systemically exposed to the assessed chemical at approximately 65 µg/kg bw/day through repeated or prolonged exposure (see **Supporting information** section). Considering the toxicology profile of the assessed chemical and the low systemic exposure level to the assessed chemical in the worst case exposure scenario, health risks from repeated exposure to the public are not expected.

This assessment does not identify any risks to public health that 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 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 0.2% concentration. The professional workers may wear some PPE (including gloves, coveralls and face masks or safety glasses). 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)
- Not bioaccumulative (Not B)
- Not toxic (Not T)

Environmental hazard classification

The assessed chemical satisfies the criteria for classification according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE, 2017) as Acute Category 3 (H402) based on the toxicity data for fish, invertebrates and algae. 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

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 may result in the release of the assessed chemical to sewers and to air.

The assessed chemical is readily degradable and is not persistent. The assessed chemical is not expected to bioaccumulate and is not expected to cause toxic effects in aquatic organisms.

As the assessed chemical is not PBT it is unlikely to have unpredictable long-term effects and its risk may be estimated by the risk quotient method ($RQ = PEC \div PNEC$). 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

The information in this statement 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)
 - coveralls
 - gloves
 - respiratory protection if exposure to vapours, mists or aerosols is possible
- 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 or the environment associated with the introduction and use of the industrial chemical can be managed.

Note:

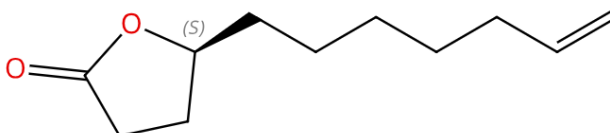
1. Obligations to report additional information about hazards under s 100 of the *Industrial Chemicals Act 2019* apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Chemical identity

Chemical name	2(3 <i>H</i>)-Furanone, 5-(6-hepten-1-yl)dihydro-, (5 <i>S</i>)-
CAS No.	3017933-60-4
Molecular formula	C ₁₁ H ₁₈ O ₂
Molecular weight (g/mol)	182.26
SMILES (isomeric)	C(CCCCC=C)[C@@H]1OC(=O)CC1

Structural formula



Chemical description

The assessed chemical has a purity greater than 95%.

Relevant physical and chemical properties

Physical form	Colourless translucent liquid
Melting point	-22.02 °C
Boiling point	305.57 °C at 101.2 kPa
Relative density (D20/4)	0.965
Vapour pressure	6.52 × 10 ⁻⁴ kPa at 25 °C (QSAR prediction)
Water solubility	1,030 mg/L at 25°C
Ionisable in the environment?	No
log K _{ow}	2.66
log K _{oc}	2.6
Flash point	162.5 °C
Auto-ignition temperature	257 °C

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 cosmetic and household products and up to 0.5% 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
Hair dye products	11,600	0.02	0.1	3
Total				63

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 approximately additional 1 µg/kg bw/day systemic exposure, considering low concentrations and retention factors for 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 m³/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 zone 1	1 minutes
Exposure duration zone 2	20 minutes
Fraction inhaled by the user	50 %
Volume zone 1	1 m ³
Volume 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 zone 1 + daily systemic exposure zone 2

Daily systemic exposure zone 1 = (amount × C × inhalation rate × exposure duration zone 1 × fraction inhaled)/volume zone 1/body weight

Daily systemic exposure 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 65 µg/kg bw/day (= 0.065 mg/kg bw/day) for the assessed chemical. Considering the hazard profile of the assessed chemical, this low level of worst-case systemic exposure is unlikely to pose a health risk to the public with repeated use of products containing the assessed chemical.

Health hazard information

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 6 female 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. 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 median lethal dose (LD50) of the chemical was determined to be greater than 2,000 mg/kg bw in female rats. 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 0.5 mL of the undiluted assessed chemical for 4 hours under semi-occlusive conditions. No erythema was noted in any test animals 1 hour after patch removal. Slight erythema (maximum score of 1) was noted in one test animal 24 hours after exposure which was reversed 48 hours after exposure. 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

Eye irritation potential of the assessed chemical was tested in rabbits following the OECD TG 405. The undiluted chemical (0.1 mL) was instilled in one eye of each of 3 female New Zealand white rabbits. The other untreated eye of the animals served as control. Mild conjunctival redness with score of 1 was observed in all 3 test animals at 24-hour after exposure. The effects were fully reversed by 48-hour after exposure. Based on the results, the assessed chemical is considered as slightly irritating to the eyes but does not meet the GHS criteria for classification as adopted by Australia for industrial chemicals.

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 12.5% concentration on day 1 and topical application at 100% concentration on day 7). After 18 days, the test animals were challenged with 25% and 50% concentrations of the assessed chemical and skin reactions were recorded 24 hours after challenge. No skin reactions attributable to allergy was observed. The assessed chemical was not a skin sensitizer under the test conditions.

Genotoxicity

The 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 WP2(uvr A-) (pKM 101) were used for the test. The chemical was tested at up to 5,000 µg/plate in the absence or presence of metabolic activation. No test substance mediated increase in the number of revertant colonies were observed under the test conditions and the assessed chemical was not considered as mutagenic.

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 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 assessed chemical is readily biodegradable (83% degradation over 28 days in OECD TG 301B study and 82.4% degradation over 28 days in OECD TG 301F study). The assessed chemical satisfied the 10-day-window criterion in both studies.

Bioaccumulation

Based on its log K_{OW} value, the assessed chemical does not have the potential to bioaccumulate.

No bioaccumulation information was provided for the assessed chemical. The experimental partition coefficient of the assessed chemical ($\log K_{OW} = 2.66$) is below 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/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 experimental median lethal concentration (LC50) and calculated median effective concentration (EC50) values for the assessed chemical in model organisms across three trophic levels were provided by the applicant:

Taxon	Endpoint	Method
Fish	96 h LC50 = 15.7 mg/L	<i>Brachydanio rerio</i> (zebrafish) OECD TG 203 Semi-static Measured concentration

Taxon	Endpoint	Method
Invertebrate	48 h EC50 = 47 mg/L	<i>Daphnia magna</i> (water flea) immobilisation iSafeRat daphEC50 v1.9 Ecotox module Calculated concentration
Algae	72 h ErC50 = 46 mg/L	<i>Pseudokirchneriella subcapitata</i> (green algae) Growth rate iSafeRat algErC50 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 > 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 experimental degradation studies, the assessed chemical is categorised as Not Persistent.

Bioaccumulation

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

Toxicity

Not Toxic (Not T). Based on available measured 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 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.

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