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

# 2*H*-Pyran, 3,6-dihydro-4-methyl-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]- 2*H*-Pyran, 5,6-dihydro-4-methyl-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]- 2*H*-Pyran, tetrahydro-4-methylene-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]-

## Assessment statement

## (CA09811/CA09864/CA09865)

**04 January 2024**

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# AICIS assessment statement (CA09811/CA09864/CA09865)

## Chemicals in this assessment

| Name | CAS registry number | Application No. |
|---|---|---|
| 2*H*-Pyran, 3,6-dihydro-4-methyl-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]- | 947237-75-4 | CA09811 |
| 2*H*-Pyran, 5,6-dihydro-4-methyl-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]- | 947237-84-5 | CA09864 |
| 2*H*-Pyran, tetrahydro-4-methylene-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]- | 947237-93-6 | CA09865 |

## Reason for the assessment

Applications for assessment certificates under section 31 of the *Industrial Chemicals Act 2019* (the Act).

### Certificate Application type

AICIS received assessment certificate applications for the three chemicals in a Very Low to Low Risk type. The chemicals will be imported together as a multi-component introduction and will not be separated during introduction or use.

## Defined scope of assessment

The chemicals have been assessed together as a multi-component introduction, manufactured together at the following concentrations and not to be separated during introduction or use:

- 2*H*-Pyran, 3,6-dihydro-4-methyl-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]- at up to 45%
- 2*H*-Pyran, 5,6-dihydro-4-methyl-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]- at up to 27%
- 2*H*-Pyran, tetrahydro-4-methylene-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]- at up to 52%.

The three components combined together are:

- Imported into Australia at up to 1 tonne/year
- Imported in fragrance formulations at up to 1% concentration for local reformulation into cosmetics and household products in:
  - leave-on and rinse-off cosmetic products including hair dye and non-spray deodorants at up to 0.05% concentration
  - washing and cleaning household products, polishes and wax blends, insecticides and repellents at up to 0.02% concentration
  - instant action air fresheners at up to 0.1% concentration

    - fine fragrances at up to 0.2% concentration
    - continuous action air fresheners at up to 1% concentration.
- Imported in finished products for sale in:
    - leave-on and rinse-off cosmetic products including hair dye and non-spray deodorants at up to 0.05% concentration
    - washing and cleaning household products, polishes and wax blends, insecticides and repellents at up to 0.02% concentration
    - instant action air fresheners at up to 0.1% concentration
    - fine fragrances at up to 0.2% concentration
    - continuous action air fresheners at up to 1% concentration.

# Summary of assessment

## Summary of introduction, use and end use

The assessed chemicals will not be manufactured in Australia. The assessed chemicals will be imported either at up to 1% concentration for further local reformulation into finished cosmetic and household products, or as fragrance component in finished end-use cosmetic and household products and fine fragrances. The cosmetic and household end use products containing the assessed chemicals are proposed to be used by professional workers under industrial or non-industrial settings, and by the general public.The end-use concentration of the assessed chemicals for consumer uses will be up to 0.05% concentration in leave-on and rinse-off cosmetic products including hair dye and non-spray deodorants, at up to 0.02% concentration in washing and cleaning household products, polishes and wax blends, insecticides and repellents, at up to 0.1% concentration in instant action air fresheners, at up to 0.2% concentration in in fine fragrances, and at up to 1% concentration in continuous action air fresheners. End-use concentration of the assessed chemicals for professional uses will be up to 0.02% concentration in washing, cleaning, disinfectant, polishes and wax blends products.

## Human health

### Summary of health hazards

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

- of low acute oral toxicity (LD50 > 2,000 mg/kg bw in rats)
- slightly irritating to skin and eyes
- not a skin sensitiser
- not considered to be genotoxic

No dermal, inhalation or repeated dose toxicity data were provided for the assessed chemicals.

### Hazard classifications relevant for worker health and safety

Based on the data provided, the assessed chemicals do not satisfy 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.

### 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 chemicals at up to 1% concentration through the use of a wide range of cosmetic and household products. The principal route of exposure will be dermal, while occular and inhalation exposures, particularly from the use of air freshener products and other products applied by spray, are also possible.

The assessed chemicals are slightly irritating to skin and eyes. However, irritation effects are not expected to occur from use of the assessed chemicals at the proposed low end use concentrations in cosmetic and household products (up to 0.2% concentration) or in air fresheners (at 1% concentration with no direct contact with skin or eyes).

No inhalation toxicity data are provided for the assessed chemicals. Due to low concentrations of the assessed chemicals in the end use products, it is not expected to pose health risk through inhalation when the assessed chemicals are used in the proposed manner.

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

**Workers**

Incidental exposure of reformulation workers to the assessed chemicals at up to 1% concentration during reformulation processes may occur predominantly via the dermal route, while ocular and inhalation exposures are also possible. To mitigate potential risks to reformulation worker from any repeated exposure, control measures would be required to minimise the exposure (see **Means for managing risk**). It is anticipated 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 reduce worker exposure.

Professional workers in cleaning or cosmetic businesses may experience exposure via dermal, inhalation and accidental ocular exposure to the assessed chemicals during the use of cleaning or cosmetic products containing the assessed chemicals at up to 0.2% concentration. The professional workers may wear PPE (including gloves, coveralls, safety glasses or face masks) to reduce exposure. 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 chemicals, requiring no specific risk management measures.

## Environment

### Summary of environmental hazard characteristics

According to domestic environmental hazard thresholds and based on the available data the chemicals are:

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

### Environmental hazard classification

The assessed chemicals satisfy the criteria for classification according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE, 2017) as Acute Category 2 (H401) and Chronic Category 2 (H411) based on the toxicity data for fish, invertebrates, and algae. Considerations were also made for the biodegradation of the assessed chemicals.

| 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 |

### Summary of environmental risk

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

The assessed chemicals are not readily biodegradable and is persistent. The assessed chemicals are predicted to degrade in the air compartment. The assessed chemicals have a low potential for bioaccumulation and are not expected to cause toxic effects in aquatic organisms.

As the assessed chemicals do not meet all three PBT criteria they are unlikely to have unpredictable long-term effects and their 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 chemicals 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 chemicals during reformulation:

- Use of engineering controls such as
  - Enclosed and automated systems where possible
  - Adequate workplace ventilation to avoid accumulation of 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 chemicals 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.

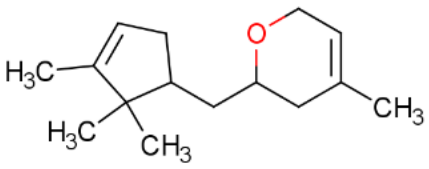
# Supporting information

## Chemical identity

**Chemical identity of CA09811**

| | |
|---|---|
| **Chemical name** | 2*H*-Pyran, 3,6-dihydro-4-methyl-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]- |
| **CAS No.** | 947237-75-4 |
| **Molecular formula** | $C_{15}H_{24}O$ |
| **Molecular weight (g/mol)** | 220.35 |
| **SMILES (canonical)** | O1CC=C(C)CC1CC2CC=C(C)C2(C)C |

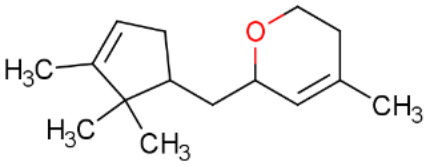
**Structural formula**




**Chemical identity of CA09864**

| | |
|---|---|
| **Chemical name** | 2*H*-Pyran, 5,6-dihydro-4-methyl-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]- |
| **CAS No.** | 947237-84-5 |
| **Molecular formula** | $C_{15}H_{24}O$ |
| **Molecular weight (g/mol)** | 220.35 |
| **SMILES (canonical)** | O1CCC(=CC1CC2CC=C(C)C2(C)C)C |

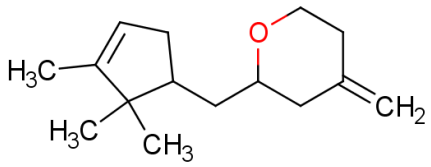
**Structural formula**



**Chemical identity of CA09865**

| | |
|---|---|
| **Chemical name** | 2*H*-Pyran, tetrahydro-4-methylene-2-[(2,2,3-trimethyl-3-cyclopenten-1-yl)methyl]- |
| **CAS No.** | 947237-93-6 |
| **Molecular formula** | $C_{15}H_{24}O$ |
| **Molecular weight (g/mol)** | 220.35 |
| **SMILES (canonical)** | O1CCC(=C)CC1CC2CC=C(C)C2(C)C |

**Structural formula**




**Chemical description**

The three chemicals in the assessment have been manufactured together and have been assessed as a multi-component introduction with a combined purity of > 90% (w/w).

# Relevant physical and chemical properties of the chemicals

| | |
|---|---|
| Physical form | liquid |
| Melting point | -81.2 °C |
| Boiling point | 276.3 °C |
| Density | 929 kg/m3 at 20 °C |
| Vapour pressure | 0.313 Pa at 20 °C |
| Water solubility | 44.4 mg/L at 25 °C (calc) |
| Flash point | 128 °C at 101.3 kPa |
| Auto flammability | 230 °C at 101.3 kPa |
| Ionisable in the environment? | No |
| pKa | 2.91-3.63 (calc) |
| log $K_{ow}$ | 3.75 at 20 °C |

# Health hazard information

## Acute toxicity

### Oral

In an acute oral toxicity study (OECD TG 423), the assessed chemicals were administered by oral gavage to 6 Sprague Dawley (SD) rats at a single dose of 2,000 mg/kg bw. A decrease in spontaneous activity was observed in 1 animal at 1 and 3 hours after administration of the assessed chemicals. No other clinical observations, mortalities and 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 dose (LD50) was determined to be greater than 2,000 mg/kg bw.

## Corrosion/Irritation

### Skin irritation

The assessed chemicals were tested in rabbits for skin irritation potential (OECD TG 404). A single 4-hour, semi-occluded application of the assessed chemicals to the intact skin of three young adult New Zealand White rabbits produced a slight to well-defined erythema (maximum score of 2) in all treated animals from the 24-hour observation until the 72-hour observation. At the 48-hour and 72-hour observations, very slight to slight oedema (maximum score of 2) was observed in all treated animals. Dryness at the test site was noted in 1 animal on Day 4 and 2 animals on Day 6 of observation. At the 14-day observation, dryness had resolved in 2 of the animals and persisted for the third animal. Therefore, under the conditions of the study, the assessed chemicals are considered slightly irritating to skin.

### Eye irritation

The eye irritation potential of the assessed chemicals was tested in three female New Zealand White rabbits (OECD TG 405). The assessed chemicals (0.1 mL) were placed into the conjunctival sac of one eye of each rabbit. The assessed chemicals produced no iridial or corneal effects. Slight to moderate conjunctival redness (maximum score of 2 at one hour observation) was noted in all treated animals. Slight redness (maximum score of 1) persisted until the 24-hour observation for 1 animal and persisted up to Days 5 and 8 of observation period in other 2 animals. Slight conjunctival chemosis (maximum score of 1) was observed in all treated animals 1 hour after treatment, resolved in 2 animals at 14 hours and persisted until Day 7 of observation for a single animal. All observed reactions in treated eyes were resolved by Day 9 of the test. Therefore, under the conditions of the study, the assessed chemicals were considered slightly irritating to the eyes.

## Sensitisation

### Skin sensitisation

In a guinea pig maximisation test (GPMT) (OECD TG 406), an intradermal induction with 25% of the assessed chemicals in olive oil was administered on 10 male Dunkin-Hartley guinea pigs followed by topical induction with 100% of the assessed chemicals. The animals were challenged with 50% and 25% of the assessed chemicals in paraffin oil. Following challenge, no skin reactions were reported in any of the treated animals. Therefore, under the conditions of the study, the assessed chemicals are not considered to be a skin sensitiser.

## Genotoxicity

A study was performed to evaluate the potential of the assessed chemicals to cause point mutations in a bacterial reverse mutation assay using *Salmonella typhimurium* strains TA98, TA100, TA102, TA1535 and TA1537 and *Escherichia coli* WP2 (pKM101) strain, in both the presence and absence of 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 concentration of the assessed chemicals, either with or without metabolic activation (S9-mix). Under the conditions of this study, the assessed chemicals were not considered to be mutagenic in the presence or absence of metabolic activation.

The assessed chemicals were also found to be non-mutagenic in an *in vitro* mammalian chromosomal aberration test using human lymphocytes, with or without metabolic activation (OECD TG 473). No statistically significant increases in the frequency of cells with aberrations were observed after 4 hours exposure period at any tested concentration, with (0.4, 8, 16, 32, 40, 48, 56, 64 µg/mL) or without (0.4, 8, 16, 32, 40, 48, 56, 56 µg/mL) metabolic activation. The assessed chemicals also showed no mutagenic properties after 24 hours exposure at any tested concentration up to 64 µg/mL, without metabolic activation.

# Environmental exposure

The assessed chemicals 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 chemicals to the environment are not expected during reformulation, transport or storage.

The assessed chemicals 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 chemicals in polish and wax blends, cosmetic products, washing, cleaning and disinfection products is expected to result in the release of the assessed chemicals “down the drain” and into the sewers. Consequently, the assessed chemicals will be treated at sewage treatment plants (STPs) before release to surface waters.

Use of the assessed chemicals in air freshener products will result in direct release of the assessed chemical into the air compartment.

## Environmental fate

### Partitioning

The partitioning of the assessed chemicals was not determined. The chemicals are treated as if they are mobile in the environment as a worst-case scenario.

### Degradation

Based on its measured degradation in water, the assessed chemicals are categorised as persistent.

The result of a supplied biodegradation study conducted using the OECD TG 301F test guideline demonstrated 2% degradation of the assessed chemicals in 28 days. The study was prolonged to 60 days to assess any further degradation, however, the assessed chemicals showed only 3% degradation in 60 days. Therefore, the assessed chemicals are not readily biodegradable in water.

The half-life of the assessed chemicals in air is calculated to be 0.744 hours, based on reactions with hydroxyl radicals (US EPA, 2012; calculated using AOPWIN v1.92). When the assessed chemicals partition to or are directly released to air, they are expected to degrade. As the half-life in air is below the domestic threshold value of 2 days, the assessed chemicals are not expected to persist in air compartment.

### Bioaccumulation

Based on its log $K_{OW}$ value, the assessed chemicals have low potential to bioaccumulate.

No bioaccumulation information was provided for the assessed chemicals. The experimental partition coefficient of the assessed chemicals (log $K_{OW}$ = 3.75) 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 chemicals are 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 chemicals 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 measured median effective concentration (EC50) values for model organisms were supplied for the assessed chemicals:

| Taxon | Endpoint | Method |
|---|---|---|
| **Fish** | 96 h LC50 = 2.7 mg/L | *Danio rerio* (Zebra fish)<br>Mortality<br>iSafeRat HA-QSAR v1.8<br>Ecotox module<br>Calculated concentration |
| **Invertebrate** | 48 h ErC50 = 1.18 mg/L | *Daphnia magna*<br>(water flea)<br>Immobilisation<br>OECD TG 202<br>Semi-static<br>Geometric mean<br>measured concentration |
| **Algae** | 72 hr ErC50 = 1.95 mg/L | *Desmodesmus subspicatus*<br>(green algae)<br>Growth rate<br>OECD TG 201<br>Static<br>Geometric mean<br>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 the chemicals 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 chemicals according to domestic environmental hazard thresholds is presented below:

## Persistence

Persistent (P). Based on a measured degradation study, the assessed chemicals are categorised as Persistent.

## Bioaccumulation

Not Bioaccumulative (Not B). Based on low measured log $K_{ow}$ value, the assessed chemicals are categorised as Not Bioaccumulative.

## Toxicity

Not Toxic (Not T). Based on available ecotoxicity calculated ecotoxicity values above 1 mg/L the assessed chemicals are categorised as Not Toxic.

# Environmental risk characterisation

Although the assessed chemicals are persistent, they do not meet all three PBT criteria. They are 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 chemicals that each exceed 0.54 mg/L.

Therefore, based on the expected RQ < 1 the assessed chemicals are not expected to pose a significant risk to the environment. As such, the environmental risks associated with the assessed chemicals 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

Struijs J (1996), SimpleTreat 3.0: a model to predict the distribution and elimination of chemicals by sewage treatment plants, National Institute of Public Health and the Environment.

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

US EPA (2012) Estimation Programs Interface (EPI) SuiteTM for Microsoft Windows®, v 4.11. US EPA. Available at https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface.