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

4,8,11-Dodecatrienal

Assessment statement (CA09558)

20 September 2022

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AICIS assessment

Chemical in this assessment

Name	CAS registry number
4,8,11-Dodecatrienal	1000399-21-2

Reason for the assessment

An application for an assessment certificate under section 31 of the *Industrial Chemicals Act 2019* (the Act).

Certificate Application type

Health focus

Based on the introduction, use and end use information described in the application, the human health and environment exposure bands of the introduction are both 2 [table item 3 Clause 1 and table item 2 Clause 3, Schedule 1 of the *Industrial Chemicals (General) Rules 2019* (the Rules)]. The assessed chemical has hazard characteristics in human health hazard band B (table items 12, clause 2, Schedule 1 of the Rules), and environment hazard band C (table item 6, clause 4, Schedule 1 of the Rules). In accordance with item 13 subsection 28(1) and item 12 subsection 29(1) of the Rules, the indicative human health risk for the proposed introduction is very low and the indicative environment risk for the proposed introduction is low. However, the application was submitted as a Health focus assessment.

Defined scope of assessment

The chemical was assessed for use by professionals and consumers as a fragrance ingredient in cosmetic, personal and household products:

- imported into Australia at up to 0.2 tonne per year
- imported at a concentration of 0.006% or less in finished end-use products

Summary of assessment

Summary of introduction, use and end use

Manufacturing, reformulation or repackaging of the assessed chemical is not expected to be performed in Australia. The assessed chemical will be imported into Australia as a fragrance ingredient in finished end-use products at up to 0.006% concentration.

The potential end-use products containing the assessed chemical are:

- Fabric and laundry: 0.005%
- Beauty care: 0.005%
- Home care: 0.001%

- Fine fragrance / perfumes: 0.006%.

The end-use products containing the assessed chemical will be widely used by professional workers including cleaners and beauty salon workers as well as consumers.

Human health

Summary of health hazards

Based on the available information, the critical health effects for risk characterisation are skin sensitisation and skin irritation.

No repeat dose toxicity data are provided on the assessed chemical.

Based on the available data the assessed chemical is

- of low oral acute toxicity;
- not expected to be irritating to eyes;
- not expected to be genotoxic.

Hazard classifications relevant for worker health and safety

The 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 follows. This does not consider classification of physical and environmental hazards.

Health hazards	Hazard category	Hazard statement
Skin sensitisation	Skin Sens. 1B	H317: May cause an allergic skin reaction
Skin corrosion / irritation	Skin Irrit. 2	H315: Causes skin irritation

Summary of health risk

Public

When introduced and used in the proposed manner, the public will be widely and repeatedly exposed to the assessed chemical through the use of cosmetic and household products containing the assessed chemical at up to 0.006% concentration.

The assessed chemical is a weak skin sensitiser and a skin irritant. Significant skin sensitisation or skin irritation effects are not expected from the use of products containing the assessed chemical at the proposed low use concentration (up to 0.006%) in cosmetic and household products.

Systemic exposure is expected to be limited by the very low concentration of the assessed chemical (up to 0.006%) in end-use products.

Overall if the assessed chemical is introduced and used in accordance with the terms of the assessment certificate (use of the assessed chemical at up to 0.006% concentration in

cosmetic and household products), no risks are identified for public health that require specific risk management measures during this assessment.

Workers

Transport, storage and retailer workers who handle the end-use products containing the assessed chemical at up to 0.006% concentration could be dermally exposed to the assessed chemical only in the unlikely event of an accidental rupture of the packaging.

Cleaners and beauty care professionals will handle the assessed chemical at up to 0.006% concentration, similar to public use. Such professionals may use personal protective equipment to minimise repeated exposure, and good hygiene practices are expected to be in place. Therefore, the risk to workers who use products containing the assessed chemical is expected to be of a similar or lesser extent than consumers who use such products on a regular basis.

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)
- Bioaccumulative (B)
- Toxic (T)

Environmental hazard classification

The chemical satisfies the criteria for classification according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE 2017) as Acute Category 1 (H400) and Chronic Category 1 (H410) based on the toxicity data for green algae. Considerations were also made for the rapid biodegradation and bioaccumulation potential of the assessed chemical.

Environmental Hazard	Hazard Category	Hazard Statement
Acute Aquatic	Acute aq. – Cat. 1	H400: Very toxic to aquatic life
Chronic Aquatic	Chronic aq. – Cat 1	H410: Very toxic to aquatic life with long lasting effects

Summary of environmental risk

The assessed chemical will be introduced as a fragrance ingredient for use in a variety of 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 has a potential to bioaccumulate and is toxic to aquatic organisms.

As the assessed chemical is not meeting 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 calculated 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

No specific means for managing risk are required when the assessed chemical is introduced in accordance with the terms of the assessment certificate.

Conclusions

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

The Executive Director is satisfied that when the 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.

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

Supporting information

Chemical identity

Chemical name	4,8,11-Dodecatrienal
CAS No.	1000399-21-2
Synonyms	Nironal™
Structural formula	
Molecular formula	$C_{12}H_{18}O$
Molecular weight (g/mol)	178.27
SMILES	O=CCCC=CCCC=CCC=C
Chemical description	The assessed chemical has a degree of purity 97.80%.

Relevant physical and chemical properties

Physical form	A clear, colourless liquid
Density	886.5 kg/m^3 at 20 °C
Melting point	No melting temperature was found between -150 °C and 50 °C
Boiling point	205.2 °C
Auto-ignition temperature	242 °C
Flashpoint	115.5 °C
Vapour pressure	1.2×10^{-3} KPa (20 °C); 1.9×10^{-3} KPa (25 °C); 1.8×10^{-2} KPa (50 °C)
Explosive Properties	Not expected
Water solubility	43 mg/L at 20 °C
Henry's law constant	0.689 Pa.m^3/mol
Ionisable in the environment?	No
log K_{ow}	4.4 at 23 °C
log K_{oc}*	3.01 at 25 °C (calc.)

*Supplied calculation performed on a representative substance (molecular weight: 178.28 g/mol) using EPI Suite version 4.11

Health hazard information

Acute toxicity

Oral

Based on an acute oral toxicity study of the assessed chemical (OECD TG 423), the assessed chemical was found to be of low acute oral toxicity in rats (LD50 > 2000 mg/kg bw).

Corrosion/Irritation

Skin irritation

The assessed chemical was determined not to be corrosive in an *in vitro* skin corrosion test using the EpiDerm™ reconstructed human epidermis tissue model (OECD TG 431). The mean relative tissue viability for the test substance was 104.2% (after 3 min exposure) and 101.3% (after 60 min exposure).

However, the assessed chemical was also determined to be irritating to the skin in an *in vitro* skin irritation test using the EPISKIN TM reconstructed human epidermis tissue model (OECD TG 439). Since the mean relative tissue viability for the assessed chemical was 9.3% (below 50%) after 1 hour treatment and a 42-hour post-incubation, the assessed chemical is considered to be a skin irritant.

Based on the available information, the assessed chemical warrants hazard classification for Skin Irritant (Category 2, H315: Causes skin irritation) according to GHS criteria as adopted in Australia for industrial chemicals.

Eye irritation

The assessed chemical was tested using reconstructed Human EpiOcular™ Cornea-like Epithelial Model (OECD TG 492) to determine whether it is not an eye irritant or requires classification for serious eye damage. The final relative mean viability of the tissues treated with the assessed chemical was 67.9% (first assay) and 82.4% (second assay) compared with the negative control. Based on these results and as per the test guideline, no prediction can be made regarding the irritant potential of the assessed chemical and further testing is required using other test guidelines.

The assessed chemical was further tested for eye irritating potential using the Bovine Corneal Opacity and Permeability (BCOP) test method (OECD TG 437). The mean In Vitro Irritancy Score (IVIS of 3.3) of the assessed chemical treated corneas did not indicate a corrosive or severe eye irritation potential in the BCOP test when compared to the IVIS of negative and positive controls (4.4 and 36.1-107.9 respectively). Under the conditions of this study, the assessed chemical did not show a corrosive or severe eye irritation potential.

Overall, based on the available information, the assessed chemical is not classified as an eye irritant.

Sensitisation

Skin sensitisation

The skin sensitisation potential of the assessed chemical was tested using a local lymph node assay (LLNA) in mice (OECD TG 429). The assessed chemical was tested at concentrations of 0, 2.5, 10 and 25%. The assessed chemical was found to be a skin sensitiser with a Stimulation Index (SI) values of 1.00, 1.26, 2.41 and 4.90 for the tested doses respectively and an EC3 value was established as 13.6%. The assessed chemical is a weak skin sensitiser, requiring classification for Skin Sensitisation (Category 1B: H317: May cause an allergic skin reaction).

Repeat dose toxicity

No repeated dose oral, dermal or inhalation toxicity data on the assessed chemical were submitted. There are no suitable analogue data.

The need for repeated dose toxicity data was waived due to the very low concentration at which the assessed chemical is introduced and used.

Genotoxicity

The assessed chemical was not mutagenic in a bacterial reverse mutation assay (OECD TG 471). There was no significant increase in revertant colony numbers of any of the tested strains of (Salmonella typhimurium TA98, TA100, TA1535, TA1537 and Escherichia coli WP2 uvrA) observed following exposed to the assessed chemical at any concentration level up to 5000 µg/plate (in the standard plate test) and up to 2500 µg/plate (in the preincubation test) under the conditions of the test, with or without metabolic activation.

No other genotoxicity data were provided.

Environmental exposure

The assessed chemical will be imported into Australia in finished personal care and household products. Significant releases of the assessed chemical to the environment are not expected during transport or storage.

The assessed chemical is a fragrance ingredient to be included in a range of products, resulting in a variety of potential exposure scenarios.

Consumer and professional uses of the assessed chemical in cosmetic products, washing products and cleaning products are 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 freshener products will result in the direct release of the assessed chemical into the air compartment.

Environmental fate

Partitioning

The assessed chemical has a moderate calculated log K_{OC} value (log K_{OC} = 3.01). Therefore, the chemical is expected to partition to soils and sediments and have low mobility.

The assessed chemical is moderately water soluble (water solubility = 43 mg/L at 20°C). If the assessed chemical is released to surface water, a proportion of the assessed chemical is expected to remain in water compartment and a proportion of the chemical is expected to partition to sediments based on its moderate water solubility and log K_{OC} value.

The assessed chemical is volatile (vapour pressure = 1.18 Pa at 20°C and 1.94 Pa at 25°C). A small proportion of the assessed chemical is expected to partition to air during STP treatment, based on SimpleTreat 3.0 model outputs (Struijs, 1996). Additionally, when the assessed chemical is directly released to air it is not expected to partition to other compartments.

Degradation

Based on its measured degradation in water and predicted degradation in air, the assessed chemical is not persistent.

The half-life of the assessed chemical in air is calculated to be 0.77 hours, based on reactions with hydroxyl radicals (US EPA, 2012; calculated using AOPWIN v1.92). As its calculated half-life in air is below the domestic threshold value of 2 days, the assessed chemical is not expected to persist in the air compartment.

Degradation studies in water indicate that the assessed chemical is readily biodegradable. The result of a biodegradation study supplied for the assessed chemical was 92% degradation (OECD 301B) over 28 days and satisfied the 10-day-window criterion.

Bioaccumulation

Based on its log K_{OW} value, the assessed chemical has potential to bioaccumulate.

No bioaccumulation information was provided for the assessed chemical. The experimental partition coefficient of the assessed chemical is log K_{OW} = 4.4, which is above the domestic bioaccumulation threshold of log K_{OW} = 4.2 (EPHC, 2009). This determination is considered to be conservative as the assessed chemical is not considered to be persistent.

Predicted environmental concentration (PEC)

A predicted environmental concentration (PEC) for Australian waters was calculated assuming 100% of the introduction volume is released into sewage treatment plants (STP). This calculated value is conservative as not all uses of the assessed chemical are expected to result in release to STP. Based on its moderate water solubility, high log Kow and biodegradability, a large proportion of the assessed chemical is expected to be removed by biodegradation and adsorption to biosolids during STP treatment. The extent to which the assessed substance is removed from the effluent in STP processes is based on its physicochemical properties, modelled by SimpleTreat 3.0 (Struijs, 1996) and is estimated to be 90%. Therefore 10% of the total introduction volume is estimated to be released to the aquatic environment. The calculation of the PEC is detailed in the table below:

Total Annual Import Volume	1000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release	2.74	kg/day
Water use	200.0	L/person/day
Population of Australia	24.386	Million
Removal within STP	90%	Mitigation
Daily effluent production	4 877	ML/day
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River	0.06	µg/L
PEC - Ocean	0.01	µg/L

These PEC values are further considered to be conservative as a portion of the calculated assessed chemical in the effluent will partition to sediments, based on the calculated log K_{OC} value of the assessed chemical.

Environmental effects

Acute toxicity

The following key measured median lethal concentration (LC50), effective concentration (EC50) and inhibition concentration (IC50) values for model organisms were supplied for the assessed chemical:

Taxon	Endpoint	Method
Fish	96 h LC50 = 3.47 mg/L	*Gobiocypris rarus* (Rare Minnow) Mortality OECD TG 203 Closed (without headspace) semi-static conditions Time-weighted mean measured concentration
Invertebrate	48 h EC50 = 2.35 mg/L	*Daphnia magna* (water flea) Immobility OECD TG 202 Closed (without headspace) semi-static conditions Arithmetic mean of the initially measured concentration
Algae	72 h ErC50 = 0.847 mg/L	*Pseudokirchneriella subcapitata* (green algae) growth rate OECD TG 201 Semi-static conditions Initially measured concentration
Microorganisms	3 h IC50 = 150 mg/L	Activated sludge from a STP Respiration inhibition OECD TG 209 Static conditions Nominal concentration

Chronic toxicity

The following measured 10th-percentile effective concentration (EC10) values for model organisms were supplied by the applicant:

Taxon	Endpoint	Method
Algae	72 h EC10 = 0.349 mg/L	*Pseudokirchneriella subcapitata* (green algae) growth rate OECD TG 201 Static conditions Initially measured concentration

Predicted no-effect concentration (PNEC)

A predicted no-effect concentration (PNEC) of 8.47 µg/L was calculated for the assessed chemical in the aquatic environment. This value was derived using the most conservative endpoint value for green algae (0.847 mg/L). An assessment factor of 100 was applied to this endpoint as acute toxicity data were provided for all three trophic levels and chronic toxicity data were provided for one tropic level (EPHC, 2009). The acute endpoint was selected, over

the algal chronic endpoint, in the absence of additional chronic endpoints to support the algal growth rate EC10 value (ECHA 2008).

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 under screening test conditions, the assessed chemical is classified as Not Persistent.

Bioaccumulation

Bioaccumulative (B). Based on the measured log K_{OW} value indicating a potential to bioaccumulate, the assessed chemical is classified as Bioaccumulative.

Toxicity

Toxic (T). Based on available acute ecotoxicity values below 1 mg/L, the assessed chemical is classified as Toxic.

Environmental risk characterisation

The assessed chemical is not a PBT chemical and is hence unlikely to have unpredictable long-term effects (EPHC 2009). An estimate of risk may therefore be determined using the risk quotient method.

Based on the PEC and PNEC values determined above, Risk Quotients (RQ = PEC ÷ PNEC) have been calculated for release of the assessed chemical to water:

Compartment	PEC	PNEC	RQ
River	0.06 µg/L	8.47 µg/L	0.007
Ocean	0.01 µg/L	8.47 µg/L	0.001

For the river and ocean compartments, an RQ less than 1 indicates that the environmental risk for the assessed chemical can likely be managed based on estimated releases, as environmental concentrations are below levels that are likely to cause harmful effects.

References

ECHA (European Chemicals Agency) (2008), Guidance on information requirements and chemical safety assessment Chapter R.10: Characterisation of dose [concentration]-response for environment, accessed 24 March 2022

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, accessed July 2022

US EPA (2012) Estimation Programs Interface (EPI) SuiteTM for Microsoft Windows®, v 4.1. [Computer software, US EPA.