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

6,10-Dodecadien-1-ol, 3,7,11-trimethyl-, (3*S*,6*E*)-

Assessment statement (OA209)

13 December 2023

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AICIS assessment (OA209)

Chemical in this assessment

Name	CAS registry number
6,10-Dodecadien-1-ol, 3,7,11-trimethyl-, (3*S*,6*E*)-	27745-36-4

Reason for the assessment

An application to vary the terms of an Inventory listing under section 88 of *the Industrial Chemicals Act 2019* (the Act).

The chemical has been previously assessed (LTD/2073) and is listed on the *Australian Inventory of Industrial Chemicals* (the Inventory). An introducer applied to vary the specific requirements to provide information (see **Supporting information**) to increase the end-use concentrations in various cosmetic and household products that exceed the current limit of 0.05%.

This assessment statement should be read in conjunction with the assessment report for LTD/2073 (NICNAS, 2019).

Defined scope of assessment

The chemical has been assessed in relation to the proposed variation to the terms of the Inventory listing.

Summary of assessment

Summary of introduction, use and end use

The assessed chemical will not be manufactured in Australia. Based on the proposed changes of circumstances related to the introduction, use and end use, it will be imported either in fragrance formulations at up to 40% concentration or in end use cosmetic and household products at various concentrations up to 40%. The proposed maximum use concentrations of the assessed chemical in the end use products are shown below:

Typical Product Type	Requested new end use concentration (%)
Body lotion	7.0
Face cream	1.7
Hand cream	1.8
Fine fragrances	1.2

Typical Product Type	Requested new end use concentration (%)
Deodorant (non-spray)	0.4
Shampoo	12.6
Conditioner	12.6
Shower gel	12.6
Hand wash soap	12.6
Hair styling products	11.7
Hair dye products	2.0
Dish washing liquid	40.0
Cleaning liquid	27.1
Laundry liquid	31.8

The cosmetic and household end-use products containing the assessed chemical may 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 new toxicological data on the assessed chemical and the toxicological data submitted for LTD/2073 (see **Supporting information**) indicate that the assessed chemical is:

- of low acute toxicity via oral route
- irritating to skin
- non irritating to eyes
- a weak skin sensitiser
- not expected to be genotoxic

No information on inhalation toxicity and repeated dose toxicity of the assessed chemical was provided. Repeated dose toxicity data from an analogue, 2,6,10-dodecatrien-1-ol, 3,7,11-trimethyl- (CAS No. 4602-84-0), was considered suitable to use (read-cross), based on the structural similarity of it to the assessed chemical. When tested in a 28-day repeated dose toxicity study, the no observed adverse effect level (NOAEL) for the analogue chemical was 1,000 mg/kg bw/day in rats (the highest dose tested). Observed effects at the highest dose included changes in the liver and kidney weights, and increased metabolising activities of the liver (CYP2E1, glutathione reductase and NADPH quinone reductase) and kidneys (glutathione-S-transferase). These effects were reversible and comparable to the control group following the 28-day recovery period (NICNAS 2016).

Hazard classifications relevant for worker health and safety

Based on the data submitted for LTD/2073, the assessed chemical satisfies the criteria for classification according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE 2017) for hazard classes relevant for worker health and safety as follows.

Health hazards	Hazard category	Hazard statement
Skin irritation	Category 2	H315: Causes skin irritation
Skin sensitisation	Category 1B	H317: May cause an allergic skin reaction

Summary of health risk

Public

There will be widespread and repeated exposure of the public to the assessed chemical at up to 40% concentration through the use of a wide range of cosmetic and household products. The principal route of exposure will be dermal, while incidental ocular and inhalation exposures are also possible. Inhalation exposure occurs particularly from the use of air care products and other products applied by spray.

The assessed chemical is a Category 2 skin irritant under GHS. However, in a newly submitted human single patch test for skin irritation (see **Supporting information)**, when tested at up to 40% concentration on human skin for 48 hours, the assessed chemical did not show any evidence of skin irritation. The end use concentration of the assessed chemical in various cosmetic products which are expected to have prolonged or repeated skin contact will not exceed 7% for leave-on cosmetics and 12.6% for rinse-off cosmetics (see **Summary of introduction, use and end use** section above). The laundry liquid, dish washing liquid and cleaning liquid may contain the chemical exceeding 12.6% concentration, however prolonged skin contact to the undiluted product is limited during these uses. On the basis of the human single patch test results, when used at up to 40% concentration in consumer products, the chemical is unlikely to cause skin irritation risk.

As described in the assessment report of LTD/2073, a risk associated with use of the assessed chemical is its potential to cause sensitisation by skin contact. When tested in an LLNA study in mice, the assessed chemical was determined to be a skin sensitiser with an EC3 value of 21.4%. With the addition of new skin sensitisation information from a human repeated insult patch test (HRIPT) (see **Supporting information**), the quantitative risk assessment (QRA) for skin sensitisation carried out previously (in LTD/2073) was revised in this assessment using the newly proposed varied concentrations in the end use products for the assessed chemical. The acceptable exposure level (AEL) was calculated using the updated safety factor of 100 (see LTD/2073 assessment report), considering the negative HRIPT results that allowed reduction of the interspecies factor from 3 to 1. The AEL calculated was 46.6 µg/cm^2/day. The AEL was greater than the derived consumer exposure levels (CELs) for all typical consumer products with higher concentrations as requested, indicating the induction of skin sensitisation risk to consumers using various products containing the assessed chemical is not expected. It is acknowledged that consumers may be exposed to multiple products containing the chemical, and a quantitative risk assessment based on aggregate exposure has not been conducted.

The health risk of repeated exposure to the assessed chemical was estimated by calculating the margin of exposure (MOE), using the worst case exposure scenario from use of multiple products simultaneously by an individual consumer. The total daily systemic exposure was estimated as 14.56 mg/kg bw/day (see **Supporting information**). Using the NOAEL of 1,000 mg/kg bw/day read-cross from the analogue chemical, MOE of 70 was calculated. Considering the conservative parameters (such as dermal absorption of 100% and simultaneous use of all the products containing the assessed chemical), with the highest dose tested in the study (with no adverse effects) for the calculation, the actual MOE is expected to be higher than the calculated value. Therefore, adverse health effects from repeated dermal exposure to the assessed chemical is not expected.

Workers

Reformulation workers

During reformulation, workers may be at risk of skin irritation and sensitisation if exposed to the assessed chemical at up to 40% concentration. It is anticipated by the applicant that the reformulation processes will involve blending operations that will be highly automated and occur in a fully enclosed/contained environment with mechanical ventilation, followed by automated filling (using sealed delivery systems) of the reformulated end-use products into containers of various sizes. The exposure of workers is further expected to be minimised through the use of personal protective equipment (PPE) such as protective clothing, eye protection and suitable gloves.

Control measures are required (see **Means for managing risk** and LTD/2073 assessment report) to minimise dermal and inhalation exposure to formulation workers.

Professional users

Professional cleaners and beauty care professionals will potentially be exposed to the assessed chemical in a variety of cosmetic and household products at ≤ 40% concentrations. Such professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using products containing the assessed chemical.

Environment

Environmental hazard classification

As described in the assessment report of LTD/2073, the data submitted warrants environmental hazard classification of the chemical according to the GHS (UNECE 2017) as presented below.

Environmental Hazard	Hazard Category	Hazard Statement
Acute Aquatic	Category 1	H400: Very toxic to aquatic life

Summary of environmental risk

The proposed variation to the terms of the Inventory listing does not impact the original environment risk assessment as the introduction volume has not changed. On the basis of the

predicted environmental concentration (PEC)/predicted no-effect concentration (PNEC) ratio and assessed use pattern, the risk of the assessed chemical to the aquatic life can be managed with the recommended control measures described in the assessment report of LTD/2073.

Means for managing risk

Inventory listing

As a result of this assessment, the following specific requirement to provide information under the **Regulatory Obligations** section of the original assessment report (LTD/2073) is varied

from:

- the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer if the concentration of the notified chemical exceeds or is intended to exceed 0.05% in cosmetic and household products

to:

- the Executive Director of AICIS must be advised in writing within 28 days by introducers, if the end use concentration of the chemical exceeds 40% in dish washing liquid, 31.8% in laundry liquid, 27.1% in cleaning liquid, 12.6% in hair shampoo, hair conditioner, shower gel and hand wash soap, 11.7% in hair styling products, 7% in body lotion, 2.0% in hair dye products, 1.8% in hand cream, 1.7% in face cream, 1.2% in fine fragrance and 0.4% in deodorant (non-spray).

Other means for managing risks related to the introduction of the chemical, as detailed in the assessment report of LTD/2073, remain unchanged (see **Recommendations** section of the LTD/2073 assessment report).

Conclusions

The conclusions of this assessment are based on the information described in the assessment report of LTD/2073 and 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 varied terms of the Inventory listing 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 are implemented.

Supporting information

Existing Australian regulatory controls

AICIS

The chemical is currently listed on the Inventory with **Specific information requirement**:

- Obligations to provide information apply. You must tell us within 28 days if the circumstances of your importation or manufacture (introduction) are different to those in our assessment.

The assessment report of the chemical (LTD/2073) states under the **Regulatory Obligation** section that the Director must be notified by an introducer in writing within 28 days:

(1) Under Section 64(1) of the *Industrial Chemicals Notification and Assessment Act 1989*; if
- the importation volume exceeds one tonne per annum notified chemical;
- the final use concentration of the notified chemical exceeds 0.05% in cosmetic and household products.

or

(2) Under Section 64(2) of the *Industrial Chemicals Notification and Assessment Act 1989*; if
- the function or use of the chemical has changed from a fragrance ingredient, or is likely to change significantly;
- the amount of chemical being introduced has increased, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health or the environment.

Under Section 75(2)(c) of the *Industrial Chemicals (Consequential Amendments and Transitional Provisions) Rules 2019* the notification obligations described above are taken to be specific requirements to provide information to the Executive Director in relation to the introduction of the industrial chemical.

Human exposure

Workers

Formulation of end products

During reformulation, dermal and ocular exposure of workers to the assessed chemical at up to 40% concentration may occur during weighing and transfer stages, blending, quality control analysis, and cleaning and maintenance of equipment. Given the low vapour pressure (9.13×10^{-6} kPa at 25 °C) of the assessed chemical, inhalation exposure of reformulation workers is not expected, unless aerosols or mists containing the chemical are formed.

The applicant states that exposure is expected to be minimised through the use of engineering controls and PPE (see LTD/2073 assessment report).

Beauty care and cleaning business

Exposure to the assessed chemical in end-use products may occur to workers where the services provided involve the application of cosmetic products (at ≤ 12.6% concentration) to clients or the use of household products (at ≤ 40% concentration) in the cleaning business. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible. Such workers may use some PPE to minimise repeated exposure and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or less extent than that experienced by consumers using products containing the assessed chemical.

Public

There will be widespread and repeated exposure of the public to the assessed chemical at up to 40% concentration through the use of a range of cosmetic and household products. The principal route of exposure will be dermal, while ocular and/or inhalation exposures are also possible, particularly if the products are applied by spray or when used in air fresheners.

Data on typical use patterns of 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 tables. For the purposes of exposure assessment, Australian use patterns for the various product categories are assumed to be similar to those in Europe. Given the low molecular weight (224.38 g/mol) of the assessed chemical, a worst-case dermal absorption (DA) rate of 100% was used along with a combined average body weight (BW) for males and females of 70 kg (enHealth 2012) for calculation purposes. 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%.

The following tables provide information on exposure estimates obtained using the above parameters.

Cosmetic products (dermal exposure from using products)

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (mg/kg bw/day)
Body lotion	7,820	7.0	1	8.55
Face cream	1,540	1.7	1	0.41
Hand cream	2,160	1.8	1	0.61
Fine fragrances	750	1.2	1	0.14
Deodorant (non-spray)	1,500	0.4	1	0.09
Shampoo	10,460	12.6	0.01	0.21
Conditioner	3,920	12.6	0.01	0.08
Shower gel	18,670	12.6	0.01	0.37
Hand wash soap	20,000	12.6	0.01	0.39

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (mg/kg bw/day)
Hair styling products	4,000	11.7	0.1	0.73
Hair dye products	11,600	2.0	0.1	0.36
Total				**11.94**

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

Household products (dermal exposure from wearing clothes)

Product type	Amount (g/use)	C (%)	Product Retained (PR) (%)	Percent Transfer (PT) (%)	Daily systemic exposure (mg/kg bw/day)
Laundry liquid	230	31.8	0.95	10	1.09
Fabric softener	90	31.8	0.95	10	0.42
Total					**1.51**

C = maximum intended concentration of assessed chemical
Daily systemic exposure = (Amount × C × PR × PT × DA)/BW

Household products (dermal exposure from using products)

Product type	Frequency (use/day)	C (%)	Product use C (g/cm^3)	Time scale factor	Daily systemic exposure (mg/kg bw/day)
Laundry liquid	1.43	31.8	0.01	0.007	0.01
Dishwashing liquid	3	40.0	0.009	0.03	0.10
All-purpose cleaner	1	27.1	1	0.007	0.59
Total					**0.70**

C = maximum intended concentration of assessed chemical
Daily systemic exposure = (Frequency × C × 1,980* × Product Use Concentration × 0.01# × Time Scale Factor × DA)/BW
* Skin contact area (cm^2)
# Film thickness on skin (cm)

Hair spray (inhalation exposure)

Amount of hairspray applied	9.89	g/day
Maximum intended concentration of the chemical	12.6	%
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	0.41	mg/kg bw/day

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

The worst-case scenario estimation using these assumptions 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 14.56 mg/kg bw/day for the assessed chemical. It is acknowledged that inhalation exposure to the assessed chemical from use of other cosmetic and household products (in addition to hair spray) may occur. However, it is considered that the combination of the conservative hair spray inhalation exposure assessment parameters, and the aggregate exposure from use of the dermally applied products, which assumes a conservative 100% dermal absorption rate, is sufficiently protective to cover additional inhalation exposure to the assessed chemical from use of other spray cosmetic and household products with lower exposure.

Health hazard information

The results from toxicological investigations conducted on the assessed chemical that were submitted with LTD/2073 assessment are summarised in the following table.

Endpoint	Test guideline	Result
Rat, acute oral toxicity	Non OECD TG study	LD50 > 2,000 mg/kg bw; low toxicity
Skin corrosion – in vitro human skin model test	OECD TG 431	non-corrosive
Skin irritation – *in vitro* reconstructed human epidermis method	OECD TG 439	irritant
Skin irritation – human closed patch test	Non OECD TG study	non irritating at 2% concentration (n = 30)
Eye irritation – *in vitro* bovine corneal opacity and permeability (BCOP) test	OECD TG 437	non irritant

Endpoint	Test guideline	Result
Mouse, skin sensitisation – Local lymph node assay (LLNA)	OECD TG 429	evidence of sensitisation (EC3 = 21.4%)
Mutagenicity – bacterial reverse mutation	Similar to OECD TG 471	non mutagenic

Additional toxicological studies conducted on the assessed chemical were provided with the variation application. The following table summarises the test guidelines used for the studies and the results obtained.

Endpoint	Test guideline	Result
Rat, acute oral toxicity	OECD TG 423	LD50 > 2,000 mg/kg bw; low toxicity
Guinea pigs, skin irritation test – 5%, 10 and 20% with phototoxicity	Non OECD TG study	Irritation effects at 10% and 20% No phototoxicity up to 20%
Skin irritation* – Human single patch test (20%, 30% and 40%; 53 test subjects)	Non OECD TG study	No evidence of dermal irritation
Skin sensitisation*# – Human Repeated Insult Patch Test (HRIPT) (20% and 40%; 109 test subjects)	Non OECD TG study	No evidence of sensitisation

* The assessed chemical was diluted in mixture of diethyl phthalate and ethanol (3:1) for the test.
# The test was conducted following shared panel method where the same test subjects were exposed to two different concentrations of the assessed chemical at the same time.

Genotoxicity

Only one study report on mutagenicity (bacterial reverse mutation test) was provided for the assessed chemical in LTD/2023. The study report indicated that the chemical was not mutagenic. No additional information on genotoxicity of the chemical was provided in this variation application. The assessed chemical does not contain any known structural alerts for genotoxicity (Derek Nexus version 6.0.1).

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