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

6,10-Dodecadienal, 3,7,11-trimethyl-, (3*S*,6*E*)-

Assessment statement (OA199)

11 December 2023

Table of contents

AICIS assessment (OA199)

Chemical in this assessment

Name	CAS registry number
6,10-Dodecadienal, 3,7,11-trimethyl-, (3*S*,6*E*)-	194934-66-2

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/1959) 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/1959 (NICNAS, 2017).

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 25% concentration or in end use cosmetic and household products at various concentrations up to 22.6%. 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	0.9
Face cream	0.7
Hand cream	0.7
Fine fragrances	0.5

Typical Product Type	Requested new end use concentration (%)
Deodorant (non-spray)	0.2
Shampoo	6.6
Conditioner	6.6
Shower gel	6.3
Hand wash soap	6.3
Hair styling products	5.0
Hair dye products	0.9
Dish washing liquid	22.6
Cleaning liquid	11.5
Laundry liquid	13.5

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 chemical and the toxicological data submitted for LTD/1959 (see **supporting information**) indicate that the assessed chemical is:

- of low acute toxicity via oral and inhalation routes
- slightly irritating to skin and eyes
- a weak skin sensitiser
- not expected to be genotoxic

No information on repeated dose toxicity of the chemical was provided. 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 with and without 28-day recovery, the analogue was determined to have a no observed adverse effect level (NOAEL) of 1,000 mg/kg bw/day in rats. Observed effects included changes in the liver and kidney weights, and increased metabolising activities of the liver (CYP2E1, glutathione reductase, 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/1959, 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 adopted for industrial chemicals in Australia as follows:

Health hazards	Hazard category	Hazard statement
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 22.6% 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 slightly irritating to the skin and eyes when tested at 100% concentration. However, the chemical is not classified for skin and eye irritation hazards under GHS criteria. Therefore, irritation effects at the proposed end-use concentrations in cosmetics are not expected.

As described in the assessment report of LTD/1959, 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 27.5%. A quantitative risk assessment (QRA) was carried out previously to assess the possibility of skin sensitisation from the use of various cosmetic and household products by consumers (LTD/1959). The QRA was revised in this assessment due to proposed changes in the end use scenarios for the assessed chemical. The calculated acceptable exposure level (AEL) of 19.82 µg/cm^2/day (for details see LTD/1959 assessment report) 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 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 3.45 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 290 was calculated. MOE greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences. Therefore, the risk of adverse effects following repeated dermal exposure from the use of various cosmetic and household products is not expected.

There are no identified risks to the public that require specific risk management measures.

Workers

Reformulation workers

During reformulation, workers may be at risk of skin sensitisation if exposed to the assessed chemical at up to 25% 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 PPE such as protective clothing, eye protection and suitable gloves.

Based on the information provided for risk assessment, the potential health effect of the assessed chemical to workers is skin sensitisation with slight skin and eye irritation. Control measures are required (see **Means for managing risk**) to manage the risk to workers. Control measures to minimise inhalation exposure may also be needed if aerosols or mists are formed during the reformulation process.

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 ≤ 22.6% 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 public consumers using products containing the assessed chemical (see above **Public** subsection).

Environment

Environmental hazard classification

As described in the assessment report of LTD/1959, 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
Chronic Aquatic	Category 1	H410: Very toxic to aquatic life with long lasting effects

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/1959.

Means for managing risk

Details on means for managing risks are described in the original assessment report of LTD/1959 (under **Recommendation** section).

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/1959) 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 22.6% in dish washing liquid, 11.5% in cleaning liquid, 13.5% in laundry liquid, 6.6% in hair shampoo and conditioner, 6.3% in shower gel and hand wash soap, 5.0% in hair styling products, 0.9% in body lotion and hair dye products, 0.7% in face cream and hand cream, 0.5% in fine fragrances, and 0.2% in deodorant (non-spray).

Other specific information requirements related to the introduction of the chemical, as detailed in the assessment report of LTD/1959, remain unchanged.

Conclusions

The conclusions of this assessment are based on the information described in the assessment report of LTD/1959 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/1959) 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 concentration of the notified chemical exceeds or is intended to exceed 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, ocular and perhaps inhalation exposure of workers to the assessed chemical at ≤ 25% concentration may occur during operations involving the assessed chemical, including transferring, weighing, blending, quality control, and cleaning and maintenance of equipment. The applicant states that exposure is expected to be minimised through the use of engineering controls such as mechanical ventilation and/or enclosed systems, and through the use of PPE including protective clothing, eye protection and suitable gloves.

Beauty care and cleaning professionals

Exposure to the assessed chemical in end-use products may occur to workers where the services provided involve the application of cosmetic products (at ≤ 6.6% concentration) to clients or the use of household products (at ≤ 22.6% 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 22.6% 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 (222.37 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	0.9	1	1.01
Face cream	1,540	0.7	1	0.15
Hand cream	2,160	0.7	1	0.22
Fine fragrances	750	0.5	1	0.05
Deodorant (non-spray)	1,500	0.2	1	0.04
Shampoo	10,460	6.6	0.01	0.10
Conditioner	3,920	6.6	0.01	0.04
Shower gel	18,670	6.3	0.01	0.17
Hand wash soap	20,000	6.3	0.01	0.18

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (mg/kg bw/day)
Hair styling products	4,000	5.0	0.1	0.29
Hair dye products	11,600	0.9	0.1	0.15
Total				**2.40**

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	13.5	0.95	10	0.42
Fabric softener	90	13.5	0.95	10	0.16
Total					**0.58**

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	13.5	0.01	0.007	< 0.01
Dishwashing liquid	3	22.6	0.009	0.03	0.05
All-purpose cleaner	1	11.5	1	0.007	0.23
Total					**0.28**

C = maximum intended concentration of assessed chemical
Daily systemic exposure = (Frequency × C × Contact area × Product Use Concentration × Film Thickness on skin × Time Scale Factor × DA)/BW
Where the contact area value is 1980 cm^2 and film thickness on skin values is 0.01

Hair spray (inhalation exposure)

Amount of hairspray applied	9.89	g/day
Maximum intended concentration of the chemical	6.6	%
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	0.19	mg/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)]

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 3.45 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/1959 are summarised in the following table.

Endpoint	Test guideline	Result
Rat, acute oral toxicity	OECD TG 420	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	OECD TG 404	slightly irritating
Rabbit, eye irritation	OECD TG 405	slightly irritating
Mouse, skin sensitisation – Local lymph node assay (LLNA)	OECD TG 429	evidence of sensitisation; EC3 = 27.5%
Mutagenicity – bacterial reverse mutation	OECD TG 471	non mutagenic
Genotoxicity – in vivo Micronucleus in mice	OECD TG 474	non genotoxic

Additional toxicological tests conducted on the assessed chemical were provided by the applicant in this assessment. The following table summarises the test guidelines used for the studies and the results obtained.

Endpoint	Test guideline	Result
Rat, acute inhalation toxicity (mist, nose only exposure for 4 hours)	OECD TG 403	LC50 > 5.19 mg/L; low toxicity
Skin irritation – Human volunteers (0.5% and 5%; 20 test subjects)	Non OECD TG study	No evidence of irritation
Skin sensitisation – Human Repeated Insult Patch Test (HRIPT) (10%; 50 test subjects)	Non OECD TG study	No evidence of sensitisation
In vitro mammalian chromosome aberration test (Chinese hamster lung fibroblast cells)	OECD TG 473	Positive for numerical aberrations but not structural aberrations
In vitro mammalian cell micronucleus test (Chinese hamster lung fibroblast cells)	Similar to OECD TG 487	Positive

Genotoxicity

In the in vitro mammalian cell chromosome aberration test using Chinese hamster lung fibroblast cells, the assessed chemical was found to be positive for clastogenic effects. When tested at doses 29.2, 34.7 and 41.3 µg/mL, the chemical induced dose-dependent increase in numerical chromosome aberrations at rates of 1.5%, 2.9% and 9.1% respectively, with 6-hour exposure in the absence of metabolic activation (S9-mix). For 24-hour exposure without S9-mix, the chemical at 27.6, 31.0 and 34.8 µg/mL dose levels induced the dose-dependent increase in numerical aberration at 14.9%, 25.9% and 42.2% respectively. No increase in numerical aberrations were observed for exposure with S9-mix. No increase in structural chromosome aberrations were noted in the study.

In the in vitro mammalian cell micronucleus test using Chinese hamster lung fibroblast cell line, the assessed chemical was found to be positive for inducing micronucleus. A dose-dependent increase of micronucleated cells was observed at 16.5, 19.7 and 23.4 µg/mL with 24-hour exposure in the absence of S9-mix, at rates of 1.9%, 2.9% and 4.0% respectively. An increase of 3.4% micronucleated cells was also observed at 33.1 µg/mL with 6-hour exposure in the absence of S9-mix; however, no dose relationship was noted in this short period exposure.

The assessed chemical contains an alkyl aldehyde functional group which is known to be reactive and may cause chromosome damage (Derek Nexus version 6.0.1). However, mammals have a family of enzymes (aldehyde dehydrogenases) that detoxify the functional group (ScienceDirect). This notion is supported by the above two studies where the genotoxic effects were not observed in the presence of metabolic activation. The in vivo genotoxicity study conducted according to the OECD TG 474 (mammalian erythrocyte micronucleus test) submitted with LTD/1959 also showed no evidence of genotoxic effects. The data collectively suggests that the chemical is not likely to be genotoxic in mammals.

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