Australian Government
Department of Health
Australian Industrial Chemicals Introduction Scheme

Galaxolide and a related polycyclic musk

Evaluation statement

14 September 2021

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AICIS evaluation statement

Subject of the evaluation

Galaxolide and a related polycyclic musk.

Chemicals in this evaluation

Name	CAS Registry Number
Cyclopenta[g]-2-benzopyran, 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethyl-	1222-05-5
1H-Naphtho[2,3-c]pyran, 3,4,6,7,8,9-hexahydro-4,6,6,9,9-pentamethyl-	1922-67-4

Reason for the evaluation

The Evaluation Selection Analysis indicated a potential risk to the environment.

Parameters of evaluation

This evaluation considers the environmental risks associated with the industrial uses of galaxolide (CAS No. 1222-05-5) and musk 89 (CAS No. 1922-67-4), two synthetic polycyclic musk fragrances. These chemicals have been assessed for their risks to the environment according to the following parameters:

- default domestic introduction volumes of 100 tonnes per annum
- industrial uses listed in the 'Summary of Use' section
- expected emission into sewage treatment plants (STPs) due to consumer and commercial use.

These chemicals have been assessed as a group as they are structurally very similar and have similar use patterns.

Summary of evaluation

Summary of introduction, use and end use

Galaxolide is a common fragrance ingredient in a variety of cosmetic and consumer use products worldwide, with a global use volume in the thousands of tonnes per year. There are no specific domestic introduction volume data available for galaxolide.

Galaxolide is used in the following products according to reported domestic and international use data:

- personal care products
- air care products
- laundry and dishwashing products

- cleaning and furniture care products
- automotive products.

No domestic or international use or introduction information was identified for musk 89. It does not appear to have widespread industrial use.

Environment

Summary of environmental hazards

According to domestic environmental hazard thresholds and based on the available data galaxolide and musk 89 are:

- Persistent (P)
- Not Bioaccumulative (not 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) for environmental hazards as follows. This does not consider classification of physical hazards and health hazards.

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

Galaxolide has global use volumes in the thousands of tonnes per year. It is used widely as a fragrance ingredient in personal care and other domestic use products and is released to wastewater as a normal part of its use pattern.

Galaxolide is toxic, has moderate bioaccumulation potential, and is categorised as persistent based on its long half-life in some soils and its degradation to persistent degradants. Primary degradation of galaxolide into galaxolidone (CAS No. 507442-49-1) and other polar degradants is rapid in a variety of environmental compartments. However, ultimate degradation of galaxolide has not been observed under environmentally relevant conditions.

A detailed analysis of the hazard characteristics of metabolites of galaxolide has not been conducted as part of this evaluation due to lack of data. However, all identified metabolites are more polar than galaxolide, and appear to be excreted rapidly by fish. These metabolites are; therefore, expected to have lower bioaccumulation potential than galaxolide, and are likely not to have PBT characteristics.

Based on measured domestic and international concentrations in sediment, STP effluent and biosolids, galaxolide is expected to be present in Australian river, sediment and soil compartments at concentrations below the level of concern.

Musk 89 is a close structural analogue of galaxolide and is expected to have similar hazard characteristics. It is not expected to be present in the Australian environment at concentrations approaching the level of concern based on its apparent lack of widespread industrial use.

Conclusions

The conclusions of this evaluation are based on the information described in the statement. Obligations to report additional information about hazards under section 100 of the *Industrial Chemicals Act 2019* apply.

The Executive Director is satisfied that the identified 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.

Although the chemicals are present at concentrations below the level of concern in the Australian environment, given the hazard characteristics of the chemicals there is a risk of adverse effects on the environment if levels increase.

Supporting information

Rationale

This evaluation considers environmental risks associated with the industrial uses of galaxolide and musk 89, two closely related synthetic tricyclic musks. The evaluation of these substances has been conducted as a group because they have known or potential applications as synthetic musk fragrances.

Galaxolide and musk 89 were developed as synthetic alternatives to natural musk chemicals (Heeringa and Beets, 1963). Galaxolide is a high production volume chemical internationally and is commonly found in personal care and household products (Reiner and Kannan, 2006). Its use in these products has potential to result in environmental exposure through emission to sewers following their use, followed by release to the environment in the treated effluents and biosolids produced by sewage treatment plants (STPs).

The Evaluation Selection Analysis (ESA) of galaxolide highlighted potential persistence, bioaccumulation, and toxicity (PBT) hazard characteristics, which indicate a high concern for the environment. This evaluation includes further refinement of the risk characterisation, and a more in-depth assessment of the available environmental hazard and exposure information for both galaxolide and its structural analogue, musk 89.

Environmental risks resulting from the use of other polycyclic musks as fragrance ingredients in Australia have previously been assessed under the former Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework established by the National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Environment Tier II assessments are available for Tonalide and Related Polycyclic Musks (NICNAS, 2016) and Celestolide and Related Polycyclic Musks (NICNAS, 2017).

Chemical identity

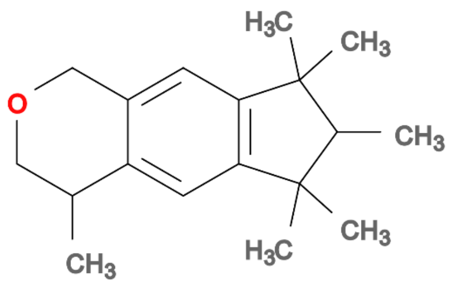
The two chemicals in this evaluation are structural isomers. Galaxolide and musk 89 are isochroman derivatives fused with an alkyl-substituted ring; galaxolide has a pentamethyl-substituted cyclopentyl ring and musk 89 has a tetramethyl-substituted cyclohexyl ring.

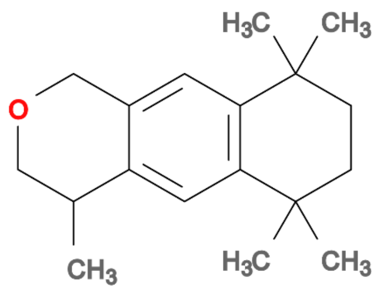
The structure of galaxolide contains two chiral centres. However, the stereochemistry of this substance is not defined in its Australian Inventory of Industrial Chemicals (Inventory) name. Technical galaxolide contains a mixture of the four stereoisomers in approximately equal proportions (Wang, et al., 2013).

The structure of musk 89 contains a single chiral centre, with its stereochemistry similarly undefined in its Inventory name. While no information was identified, it is assumed that technical mixtures of musk 89 are composed of a racemic (equal) mixture of two enantiomers.

Purified galaxolide (mixture of stereoisomers) is a crystalline solid whereas the technical mixture is a viscous liquid. The technical mixture has a purity of 70–80%, and is sold under the same name and CAS No. as its major component. The remaining 20–30% comprises four structural isomers of galaxolide that are by-products of the synthetic procedure. A typical mixture contains 6–16% of two isomers combined that each contain an ethyl group on the cyclopentyl ring in one of two possible positions (CAS Nos. 78448-48-3 and 78448-49-4), and 4–16% of two isomers combined that differ from galaxolide in the position of the fused cyclopentyl ring (CAS Nos. 114109-63-6 and 114109-62-5) (ECB, 2008; HERA, 2004; Sprecker, 1987). None of these structural isomers are listed on the Inventory. Musk 89 is synthesised via a distinct synthetic procedure and is not an impurity in the galaxolide technical mixture.

Due to difficulties using the viscous technical galaxolide in formulating fragrance blends, galaxolide is available commercially as a solution containing 65 parts by weight of the technical mixture and 35 parts by weight of solvent. Common solvents include diethyl phthalate (DEP, CAS No. 84-66-2), benzyl benzoate (BB, CAS No. 120-51-4) and isopropyl myristate (IPM, CAS No. 110-27-0). The resulting solutions are referred to as galaxolide 50 DEP, BB or IPM, respectively, with the '50' referring to the percentage of pure galaxolide (ECB, 2008).

CAS	1222-05-5
Chemical name	cyclopenta[*g*]-2-benzopyran, 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethyl-
Synonyms	galaxolide HHCB abbalide pearlide chromanolide hexamethylindanopyran
Structural formula	
Molecular formula	$C_{18}H_{26}O$
Molecular weight (g/mol)	258.4
SMILES	C1(C)(C)c2c(C(C)(C)C1C)cc1c(C(C)COC1)c2
Chemical description	N/A

CAS	1922-67-4
Chemical name	1*H*-naphtho[2,3-*c*]pyran, 3,4,6,7,8,9-hexahydro-4,6,6,9,9-pentamethyl-
Synonyms	musk 89
Structural formula	
Molecular formula	$C_{18}H_{26}O$
Molecular weight (g/mol)	258.4
SMILES	C1=C3C(=CC2=C1COCC2C)C(CCC3(C)C)(C)C
Chemical description	N/A

Relevant physical and chemical properties

Measured physical and chemical property data for galaxolide were retrieved from the registration dossier for the chemical submitted under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) legislation in the European Union (EU) (REACH, 2011), the EU Risk Assessment Report (EU RAR) for galaxolide (ECB, 2008) and the patent literature (Heeringa and Beets, 1963).

There are few measured values available for the physical and chemical properties of musk 89. The melting point was retrieved from the patent literature (Heeringa and Beets, 1963); the values for other chemical properties were calculated using standard quantitative structure-property relationships (QSPR); and the Henry's Law constant was calculated from determined values for water solubility and vapour pressure (US EPA, 2017a):

Chemical	Galaxolide	Musk 89
Physical form	Solid	Solid
Melting point	53.0–53.5°C (exp.)	44.7–45.4°C (exp.)
Boiling point	318°C (exp.)	330°C (calc.)
Vapour pressure	0.0727 Pa (exp.)	0.0341 Pa (calc.)
Water solubility	1.75 mg/L (exp.)	0.11 mg/L (calc.)
Henry's Law constant	36.9 Pa·m^3/mol (exp.)	80.2 Pa·m^3/mol (calc.)
Ionisable in the environment?	No	No
pK_a	N/A	N/A
log K_{ow}	5.9 (exp.)	6.3 (calc.)

Information is not available on whether the test substance used for measurements of physical and chemical properties was pure crystalline galaxolide or the liquid technical mixture. It is likely that melting point measurements were made on the purified material, since the technical mixture is a liquid at room temperature. For all other measured data, including standard tests on environmental hazard characteristics, the precise nature of the galaxolide test material is unknown and is a source of uncertainty in this evaluation.

Since musk 89 is a close structural analogue of galaxolide with similar physical and chemical properties, galaxolide is considered a suitable read-across analogue for determination of the hazard characteristics of musk 89.

Introduction and use

Australia

No specific Australian import or manufacturing information has been identified for galaxolide or musk 89. No specific Australian use has been identified for musk 89.

Galaxolide has reported domestic use in cleaning products, and in marine and automotive aftermarket products such as coatings (NICNAS, 2019). Based on information in the public domain, galaxolide is readily available for use in Australia as a fragrance ingredient (Australian Botanical Products, 2020).

International

Available information indicates that galaxolide is used at high volumes as a fragrance ingredient in a range of products worldwide. Musk 89 does not appear to have widespread industrial use.

Galaxolide is used in the EU in the range of 1000–10,000 tonnes per year (t/year) (REACH, 2011). In the United States of America (USA) galaxolide is listed as a high production volume chemical (US EPA, 2020b), with an annual use volume of 454–4,536 tonnes (US EPA, 2016). In the Nordic countries, the average annual use volume over a five-year period from 2014–2018 was 22 tonnes (SPIN, 2018).

Galaxolide is listed on the International Fragrance Association (IFRA) transparency list, which identifies chemicals used as fragrances by member companies (IFRA, 2020). Galaxolide is used as a fragrance ingredient in consumer products as both a base-note scent and a fixative chemical to prolong the exposure of more highly volatile fragrances (Cella and Cella, 1992; Correia, et al., 2013). Galaxolide has been measured in perfumes at concentrations up to 15 milligrams per gram (mg/g), equating to 1.5% (w/w) (Nakata, et al., 2015).

A USA-based study found and quantified galaxolide in 43 of 60 household and personal care products surveyed, with the highest concentrations found in perfumes and fragrances (up to 5.0 mg/g), body lotions and moisturisers (up to 3.7 mg/g) and deodorants (up to 2.3 mg/g) (Reiner and Kannan, 2006). Other products that contain galaxolide include body wash, shaving cream, shampoo, conditioner, hair gel, soap, cosmetics, air fresheners, scented candles, fabric softener, detergent, polishes and surface cleaners (Nakata, et al., 2015; US EPA, 2020a).

Galaxolide has non-industrial use as a fixative in pesticides to lengthen their exposure time (Bessette, 2001; US EPA, 2020a). The use of this chemical as a pesticide additive is beyond the scope of this evaluation.

No specific international use, import or manufacturing information has been identified for musk 89. It is listed on the European Commission's cosmetic ingredients database (CosIng) as a perfuming agent (European Commission, 2020). However, it is not registered under the EU REACH legislation and is 'inactive' on the US Environmental Protection Agency (US EPA) chemical substance inventory (ECHA, 2020; US EPA, 2020c). The chemical is not listed on the IFRA transparency list or as an ingredient in products on the chemical and product categories (CPCat) database (IFRA, 2020; US EPA, 2015). Musk 89 does not appear to have widespread industrial use internationally.

Existing Australian regulatory controls

Environment

The use of galaxolide and musk 89 is not subject to any specific national environmental regulations.

International regulatory status

United Nations

Galaxolide and musk 89 are not currently identified as persistent organic pollutants (POPs) (UNEP, 2001), ozone depleting substances (UNEP, 1987), or hazardous substances for the purpose of international trade (UNEP & FAO, 1998).

United States of America

Galaxolide was assessed in 2014 under the US EPA's work plan. The assessment concluded that the chemical posed no unacceptable risk to the environment at current environmental exposure concentrations (US EPA, 2014).

Environmental exposure

Galaxolide is expected to be found in household and commercial products available for use in Australia. It is used as a fragrance ingredient internationally and formulated products on the Australian market are assumed not to differ significantly from those available internationally. International studies have measured galaxolide in perfumes and fragrances, personal care products (shampoo, conditioner, soap, deodorant, body lotion, moisturiser, hair gel), and household cleaners (laundry detergent, fabric softener, surface cleaner) at concentrations up to 1.5% (w/w) (Nakata, et al., 2015; Reiner and Kannan, 2006). Chemicals used in cosmetics, personal care and cleaning products are typically released to wastewater as a normal part of their use in household and industrial applications.

Depending on degradation and partitioning processes of chemicals in sewage treatment plants (STPs), some fraction of the quantity of chemicals in wastewater entering STPs can be emitted to the air compartment, to rivers or oceans in treated effluent, or to soil by application of biosolids to agricultural land (Struijs, 1996). The emissions of galaxolide and musk 89 to environmental surface waters, sediment, and soil are considered as part of this evaluation.

Environmental fate

Partitioning

Galaxolide partitions to water, sediment and soil when released to the environment.

Galaxolide is a neutral organic chemical that is expected to be slightly soluble in water and moderately volatile. The Henry's Law constant of this chemical (36.9 $Pa{\cdot}m^3/mol$) indicates it will be moderately volatile from water and moist soil. Galaxolide is a lipophilic chemical with a measured log K_{OW} of 5.9 and a calculated soil adsorption coefficient (log K_{OC} = 4.29 L/kg), indicating that it will be immobile in soil and will preferentially adsorb to phases in the environment with high organic carbon content (including sediment and soil) (REACH, 2011; US EPA, 2017a).

Galaxolide may be emitted to the soil compartment through application of biosolids from STP processes. Calculations with a standard multimedia partitioning (fugacity) model with sole release to the soil compartment (Level III approach) predict that galaxolide will predominately be found in soil (99.9%) (US EPA, 2017a).

Galaxolide is expected to be released to the water compartment in STP effluent as a result of its use. Fugacity calculations (Level III approach) assuming sole release to the aquatic environment predict that galaxolide will primarily be found in the water (40.6%) and sediment (58.8%) compartments (US EPA, 2017a). A die-away study measured the volatilisation of galaxolide from river water and found that 17% of the initial loading volatilised over 28 days, giving a volatilisation half-life on the order of months (ECB, 2008).

Musk 89 is a neutral organic chemical that is expected to be slightly soluble in water and moderately volatile. The Henry's Law constant of this chemical (80.2 Pa·m3/mol, calc.) indicates the chemical will be moderately volatile from water and moist soil. Musk 89 is a lipophilic chemical with a calculated log K_{OW} of 6.3 and a calculated log K_{OC} of 4.3, which indicates it will be immobile in soil and will preferentially adsorb to phases in the environment with high organic carbon content (including sediment and soil) (US EPA, 2017a). Fugacity calculations predict that the partitioning behaviour of musk 89 will not significantly differ from galaxolide.

Degradation

Galaxolide is persistent in some soil types. It undergoes primary degradation in water, soil and sediment to persistent degradants.

Calculations from standard QSARs predict that galaxolide will degrade rapidly in air following reaction with hydroxyl radicals with a half-life of 3.33 hours (US EPA, 2017a). Galaxolide has no hydrolysable functional groups and is not expected to degrade by hydrolysis in the water compartment.

Galaxolide is not readily biodegradable based on a study conducted according to OECD test guideline (TG) 301B (REACH, 2011). The chemical did not mineralise under screening test timeframes (0% CO_2 release in 28 days). A second test was conducted under the same test guidelines, using pre-adapted inoculum that had been exposed to galaxolide for 8 weeks prior. No evidence of biodegradation was observed (REACH, 2011).

Galaxolide undergoes primary degradation in water, sediment, biosolids and soil, with no evidence of ultimate degradation under environmentally relevant conditions.

The primary degradation half-life of galaxolide in river water inoculated with activated sludge was measured in a study to be 33–100 hours (ECB, 2008). After 28 days only 8% of the parent remained and the balance was accounted for by volatilisation (16%) and polar metabolites (62%). One commonly detected metabolite in the environment is galaxolidone (CAS RN 507442-49-1) (Bester, 2004; Cunha, et al., 2015; Kupper, et al., 2004; Reiner and Kannan, 2011; Vallecillos, et al., 2014). Experiments have shown that galaxolidone is not persistent itself, but it does appear to degrade more slowly than galaxolide (Poulsen and Bester, 2010). Other studies have identified methoxylated and hydroxylated metabolites of galaxolide (ECB, 2008; Martin, et al., 2007).

Galaxolide has an expected primary degradation half-life in sediment of 79 days. Sediment samples were spiked with radiolabelled galaxolide, sealed and incubated for a year. After one year, 4% of the parent galaxolide remained in the sediment, giving a primary degradation half-life of 79 days. After completion of the study there was an 80% recovery of original radioactivity from the sediment by solvent extraction, which is expected to comprise mostly polar oxidised metabolites (ECB, 2008).

Galaxolide is expected to degrade in soils with a primary degradation half-life of 95–239 days, depending on the soil type (ECB, 2008). Samples of oak forest soil, agricultural soil and STP sludge-amended agricultural soil were spiked with radiolabelled galaxolide, sealed in flasks and incubated for a year. The degradation half-lives of galaxolide were determined to be 95, 239, and 105 days for oak forest soil, agricultural soil, and sludge-amended soil, respectively. In the sludge-amended soil the total recovery of radiolabelled material was 73%, comprising galaxolide (9%) and polar degradants. An additional 20% of radiolabelled material was recovered after treatment by a process to detach covalently bound degradants from organic components in the soil. Therefore, galaxolide may degrade in soil with a half-life exceeding the domestic categorisation threshold for persistence (EPHC, 2009).

Studies with pure fungal cultures show that some mineralisation may occur under idealised and not environmentally relevant conditions. A study was conducted to isolate highly active fungal strains from 64 soil samples, and resulting pure fungal cultures were tested for their capacity to degrade radiolabelled galaxolide. In cultures of *Phanerochaete chrysosporium* (a white rot fungus) galaxolide disappeared within 3 days, whereas in *Cladosporium cladosporiodes* (one of the most common fungi in outdoor air world-wide) 95% of galaxolide disappeared within 4 weeks (ECB, 2008). The detected metabolites were more polar than the parent and comprised galaxolidone (19%) and other uncharacterised degradants (75%). Evidence of partial mineralisation to CO_2 was observed after an extended period, with 82% of total radioactivity recovered from organic and aqueous extractions, and 18% recovered as CO_2 after 200 days. The mineralisation half-life under these idealised conditions would, therefore, still exceed domestic categorisation thresholds (EPHC, 2009).

No studies on the degradation of musk 89 have been identified but the chemical is expected to be persistent based on standard QSARs (US EPA, 2017a), with predicted primary and ultimate half-lives of 7.6 months and more than 10 years, respectively (LMC, 2015).

Bioaccumulation

Galaxolide and musk 89 have a moderate potential to bioaccumulate in aquatic life and an uncertain potential to bioaccumulate in benthic organisms. Metabolites of galaxolide are more polar than the parent chemical and are not expected to bioaccumulate.

Experimentally determined bioconcentration factors (BCFs) are below the domestic categorisation threshold for bioaccumulation (BCF ≥2000 L/kg) (EPHC, 2009). Two bioconcentration studies have been conducted in accordance with OECD TG 305E; a BCF of 1584 litres per kilogram (L/kg) wet weight (wwt) was reported for *Lepomis macrochirus* (bluegill sunfish) (REACH, 2011), and a BCF of 1660 L/kg wwt was reported for *Danio rerio* (Balk, et al., 2001). The BCF for the latter study was calculated from the lipid-only BCF, normalised to 5% lipid weight. Non-standard studies in the scientific literature report BCFs in the range of 201–1561 L/kg wwt (Blum, et al., 2018; Fromme, et al., 2001; Schreurs, et al., 2004) and bioaccumulation factors (BAFs) in the range 18–371 L/kg wwt (Reiner and Kannan, 2011).

There is some evidence to suggest that galaxolide has a higher bioaccumulation potential in some sediment-dwelling organisms. One study exposed *Lumbriculus variegatus* (blackworm) to galaxolide in a water-only test vessel, deriving a BCF value of 2692 L/kg wwt (Artola-Garicano, et al., 2003). Tests were also conducted with *Chironomus riparius* larvae (midge), deriving a BCF of 85 L/kg. Since these tests were not conducted in mixed sediment-water systems it is not possible to conclude if these bioconcentration values are environmentally relevant.

There are limited data available to evaluate the bioaccumulation potential of the metabolites of galaxolide. However, metabolites are each expected to be more polar than galaxolide and may be cleared from aquatic organisms quite rapidly (ECB, 2008; Fernandes, et al., 2013; Martin, et al., 2007). During the principal OECD TG 305E bioconcentration study for galaxolide with *L. macrochirus*, it was estimated that galaxolide was metabolised and the metabolite(s) excreted with a turnover rate of 38–50% per day (ECB, 2008).

Musk 89 is not expected to be bioaccumulative based on calculations with standard QSPRs that predict a BCF of 1156 L/kg, which is below the domestic categorisation threshold.

Environmental transport

Galaxolide may undergo long-range transport. Galaxolide has been identified in remote pristine environmental areas in biota, air, surface water and snow samples.

Despite a short predicted atmospheric lifetime of 3.3–5.3 hours (Aschmann, et al., 2001), environmental monitoring has identified galaxolide in pristine environmental areas that do not receive direct anthropogenic outputs. Galaxolide was found in fish caught at remote alpine lakes in Switzerland in concentrations of 0.042–0.078 milligrams per kilogram (mg/kg) lipid weight (Schmid, et al., 2007). Atmospheric concentrations of galaxolide were measured in the North Sea and Arctic regions in concentrations ranging from 5–49 picograms per cubic metre (pg/m^3) and 1–9 pg/m^3, respectively. Surface water concentrations in the North Sea ranged from 12–2030 picograms per litre (pg/L), with quantities in the ocean decreasing with distance from the mainland in a north/northeast direction (none detected in samples from the northeast Atlantic or Arctic) (Xie, et al., 2007). Galaxolide has also been measured in snow samples collected from a remote glacier in the Italian Alps, in concentrations of 2.13–5.07 ng/L (Villa, et al., 2014).

Predicted environmental concentration (PEC)

The concentration of galaxolide in Australian river water is estimated to be 2.0 micrograms per litre (µg/L) based on domestic monitoring data, with a worst-case concentration of 4.6 µg/L. Reasonable worst-case concentrations of galaxolide in domestic sediments and soil are predicted to be 0.38 mg/kg dry weight (dw) and 0.11 mg/kg dw respectively. These values were determined by considering available domestic and international monitoring data for galaxolide in wastewater effluents, biosolids, sediments, surface waters and biota. No environmental monitoring data for musk 89 were identified and a PEC has not been determined.

The highest galaxolide concentrations in the Australian environment were measured at sewage outfall sites in Darwin Harbour in 2010–2011. The maximum concentration measured was 2.0 µg/L, detected in the outfall from East Point STP in October 2010 (late dry season), an advanced primary treatment plant that treats urban sewage from Darwin city. Treated effluent is released 150 m offshore into Darwin Harbour, and samples were collected near the discharge pipe at low tide to minimise dilution. Concentrations of 0.1–0.5 µg/L were measured at other sites near Darwin at different times of the year (French, et al., 2015). The value of 2.0 µg/L in surface water is taken as the estimated galaxolide surface water concentration in Australia for the purposes of risk characterisation.

A recent domestic study tracked galaxolide through an advanced water treatment plant in Sydney, NSW (Wang and Khan, 2014). The study reported an average influent concentration of 2.55 µg/L that reduced to 1.19 µg/L after secondary treatment (moving bed biofilm reactor and membrane bioreactor), and 0.021 µg/L after tertiary treatment (reverse osmosis and disinfection, 99% total removal efficiency).

Galaxolide has also been detected in STP influent and effluent internationally. The removal efficiency following secondary and tertiary treatment is consistent with measured values in Australia. Influent concentrations up to 45.1 µg/L have been measured internationally (Vallecillos, et al., 2014), but values are more frequently in the range of 0.5–10 µg/L (Bester, 2004; Clara, et al., 2011; Ramírez, et al., 2011; Simonich, et al., 2002; Smyth, et al., 2007). Effluent concentrations largely depend on the level of treatment available, with concentrations of *ca* 0.2–4.6 µg/L measured following secondary treatment (Bester, 2004; Buerge, et al., 2003; Clara, et al., 2011; Ramírez, et al., 2011; Simonich, et al., 2002; Smyth, et al., 2007; Vallecillos, et al., 2014; Wong, et al., 2019) and concentrations of 0.0015–0.042

µg/L measured following tertiary treatment (Ramírez, et al., 2011; Vallecillos, et al., 2014). The value of 4.6 µg/L in effluent after secondary treatment is taken as a worst-case surface water concentration in Australia.

International studies have quantified galaxolide in surface waters (rivers and lakes) in concentrations up to 3.15 µg/L (Blum, et al., 2018; Buerge, et al., 2003; Clara, et al., 2011; Fromme, et al., 2001; Oros, et al., 2003; Ramírez, et al., 2011; Wong, et al., 2019). An extensive analysis of surface waters in Germany reported a 90th percentile galaxolide concentration of 0.46 µg/L (OSPAR Commission, 2004). Concentrations tend to be higher in urban area waterways and those impacted by sewage outfall (Fromme, et al., 2001; Wong, et al., 2019).

A study of sediment contamination in Berlin (Germany) rivers reported a 90th percentile galaxolide concentration of 0.38 mg/kg dw from a river moderately contaminated with biosolids, and a maximum concentration of 2.20 mg/kg from a heavily contaminated river (Fromme, et al., 2001). Galaxolide has been measured in concentrations up to 0.27 mg/kg dw in sediment samples from Europe (Sweden and Austria) and China (Pearl River estuary) (Blum, et al., 2018; Clara, et al., 2011; Huang, et al., 2016). A value of 0.38 mg/kg dw has been used as the concentration of galaxolide in sediments in Australia for the purposes of risk characterisation and 2.20 mg/kg dw is considered a worst-case PEC for the purposes of this evaluation.

Measured concentrations of galaxolide in biosolids range of 0.25–177 mg/kg dw internationally (Bester, 2004; Clara, et al., 2011; DiFrancesco, et al., 2004; Kupper, et al., 2004; Langdon, et al., 2010; Mogensen, et al., 2004). Mean and median values of 14.0 and 10.7 mg/kg dw, respectively, were determined in a literature review of biosolids contaminants (Langdon, et al., 2010).

The calculated galaxolide concentration in soil amended with biosolids is 0.11 mg/kg dw based on mean measured international biosolid concentrations (14 mg/kg dw), typical biosolids application rates and a soil bulk density of 1300 kilograms per cubic metre (kg/m^3) (EPHC, 2009; Langdon, et al., 2010). A maximum concentration of 5.5 mg/kg dw was calculated using the maximum measured concentration of galaxolide in biosolids and maximum biosolids application rates.

Galaxolide has been found in aquatic biota internationally. Galaxolide has been detected in perch (0.0067–0.13 mg/kg wwt, 0.69–27 mg/kg lipid weight) (Blum, et al., 2018; Törneman and SWECO Environment, 2008), eel (up to 4.8 mg/kg wwt, 18.48 mg/kg lipid weight) (Fromme, et al., 2001), mullet and flounder (up to 0.012 mg/kg dw), mussels (up to 0.035 mg/kg dw) and clams (0.033 mg/kg dw) (Cunha, et al., 2015; Törneman and SWECO Environment, 2008). A study by Fromme and co-workers correlated the concentration of galaxolide in eels with the extent of river contamination from STP effluent. Areas with low, medium and high contamination had average concentrations of 0.052, 0.12 and 1.51 mg/kg wwt, respectively (Fromme, et al., 2001).

Environmental concentrations of musk 89 have not been estimated using default introduction volumes. Based on available information, musk 89 does not have widespread industrial use. If musk 89 is used as a fragrance ingredient domestically it is only expected to be used in small volumes resulting in limited environmental emissions.

Environmental effects

Effects on aquatic life

Galaxolide and musk 89 are expected to cause toxic effects at low concentrations in aquatic organisms across multiple trophic levels.

No experimental data for the ecotoxicity of musk 89 were identified. The ecotoxicity data presented below for galaxolide is expected to be suitable for read-across to musk 89 given the structural similarity of the two chemicals and expected baseline narcosis mode of toxic action for both chemicals (LMC, 2020; US EPA, 2017b).

Acute toxicity

The following measured median lethal concentration (LC50) and median effective concentration (EC50) values for model organisms across 3 trophic levels exposed to galaxolide were retrieved from the scientific literature or the registration dossier for galaxolide under EU REACH legislation (REACH, 2011; Yamauchi, et al., 2008):

Taxon	Endpoint	Method
Fish	96 h LC50 = 0.95 mg/L	*Oryzias latipes* larvae (Japanese rice fish) Test substance was dissolved in 0.1% DMSO OECD TG 203 equivalent
	96 h LC50 = 1.36 mg/L	*Lepomis macrochirus* (bluegill sunfish) Flow-through conditions OECD TG 204
Invertebrate	48 h EC50 = 0.3 mg/L	*Daphnia magna* (water flea) Mobility OECD TG 202
Algae	72 h EC50 = 0.72 mg/L	*Pseudokirchneriella subcapitata* (microalgae) Biomass OECD TG 201

Chronic toxicity

The following measured no-observed-effect concentrations (NOEC) for model organisms across 3 trophic levels were retrieved from the scientific and regulatory literature, or the registration dossier for galaxolide under EU REACH legislation (Balk and Ford, 1999; REACH, 2011):

Taxon	Endpoint	Method
Fish	36 d NOEC = 0.068 mg/L	*Pimephales promelas* eggs (fathead minnow) Larval survival and growth Flow-through conditions OECD TG 210
	21 d NOEC = 0.093 mg/L	*Lepomis macrochirus* (bluegill sunfish) Growth Flow-through conditions OECD TG 204 (extended to 21 d)
Invertebrate	21 d NOEC = 0.111 mg/L	*Daphnia magna* (water flea) Reproduction Semi-static conditions OECD TG 202
Algae	72 h NOEC = 0.201 mg/L	*Pseudokirchneriella subcapitata* (microalgae) Growth Static conditions OECD TG 201

Marine chronic toxicity

The following measured effective concentration at 10% inhibition (EC10) value for a model invertebrate organism exposed to galaxolide were retrieved from the registration dossier for the chemical under EU REACH legislation (REACH, 2011):

Taxon	Endpoint	Method
Invertebrate	5–6 d EC10 = 0.0438 mg/L	*Acartia tonsa* (marine copepod) Larval development rate OECD Draft Guideline

Galaxolide saturates efflux transporters in the gills of the marine mussel *Mytilus californianus,* impeding their ability to eject xenobiotic substances from cells and raising concern that galaxolide might enhance the toxicity of other chemicals. Inhibition was observed for 24–48 hours following a 2 hour exposure to galaxolide, with a median inhibitory concentration (IC50) of 0.63 mg/L (2.43 µM) (Luckenbach and Epel, 2005). Insufficient data are currently available to evaluate the potential for this effect to cause adverse outcomes in organisms exposed to galaxolide in the environment.

Effects on sediment dwelling life

Galaxolide can cause toxic effects in sediment-dwelling organisms at low concentrations.

Sediment-dwelling acute toxicity

The following measured LC50 value for amphipods exposed to galaxolide in sediment were retrieved from the Registration Dossier for the chemical under EU REACH legislation (REACH, 2011):

Taxon	Endpoint	Method
Amphipod	96 h LC50 = 62.5 mg/kg dw	*Hyalella azteca* (scud) OECD TG 218

Sediment-dwelling chronic toxicity

The following NOEC values for three model organisms exposed to galaxolide in sediments were retrieved from the Registration Dossier for the chemical under EU REACH legislation (REACH, 2011):

Taxon	Endpoint	Method
Midge	28 d NOEC = 250 mg/kg dw	*Chironomus riparius* (harlequin fly) Emergence rate OECD TG 218
Worm	28 d NOEC = 16.2 mg/kg dw	*Lumbriculus variegatus* (blackworm) Reproduction OECD TG 218
Amphipod	28 d NOEC = 7.1 mg/kg dw	*Hyalella azteca* (scud) Growth OECD TG 218

Effects on terrestrial life

Galaxolide can cause toxic effects in terrestrial organisms.

Chronic ecotoxicity values have been obtained for the springtail *Folsomia candida* and the earthworm *Eisenia fetida* exposed to galaxolide in standard soil with 10% added organic matter (sphagnum peat). Both studies were conducted according to ISO test guidelines. A 28 day NOEC of 45 mg/kg dw (survival) was obtained for *F. candida*, and for *E. fetida* a 56 day NOEC (reproduction) of 45 mg/kg dw and a 28 day NOEC (growth) of 105 mg/kg dw were obtained (REACH, 2011).

Endocrine effects/activity

Galaxolide has some endocrine activity at the biochemical level in fish. However, no apical effects have been observed as a result of endocrine activity.

Galaxolide exposure at 0.5 mg/L induced higher levels of hepatic vitellogenin in medaka (*Oryzias latipes*), indicating some oestrogenic activity (Yamauchi, et al., 2008). Galaxolide has also exhibited anti-oestrogenic activity; when co-injected with estradiol in rainbow trout (*Oncorhynchus mykiss*), plasma levels of vitellogenin decreased (Simmons, et al., 2010). In vitro studies have also measured an anti-oestrogenic response against fish estrogen receptors (Schreurs, et al., 2004; Simmons, et al., 2010).

Predicted no-effect concentration (PNEC)

A freshwater PNEC for galaxolide of 6.8 µg/L was derived from the measured fish chronic ecotoxicity endpoint (36 d NOEC = 0.068 mg/L) using an assessment factor of 10. This assessment factor was selected as reliable chronic ecotoxicity data are available over 3 trophic levels (EPHC, 2009).

A soil PNEC of 0.31 mg/kg dw was derived from the measured springtail chronic ecotoxicity endpoint (28 d NOEC = 45 mg/kg dw). Following the approach used in the EU Risk Assessment Report, the NOEC for *F. candida* was first normalised to a soil organic content of 3.4% (ECB, 2008). An assessment factor of 50 was then applied, selected because reliable chronic ecotoxicity data are available over 2 taxa (EPHC, 2009).

A sediment PNEC of 1.58 mg/kg dw was derived from the measured amphipod chronic ecotoxicity endpoint (28 d NOEC = 7.1 mg/kg dw). Following the approach above, the NOEC for *H. azteca* was first normalised to a sediment organic content of 4% (EPHC, 2009). An assessment factor of 10 was then applied, selected because reliable chronic ecotoxicity data are available over 3 taxa.

Categorisation of environmental hazard

The categorisation of the environmental hazards of the assessed chemicals according to domestic environmental hazard thresholds is presented below (EPHC, 2009):

Persistence

Persistent (P). Based on results from standard biodegradability tests that show no evidence of ultimate degradation and evidence that galaxolide degrades to persistent metabolites, galaxolide and musk 89 are categorised as Persistent in sediment and water. Based on results from degradation studies that report a primary half-life that exceeds 180 days in some soil types, galaxolide and musk 89 are categorised as Persistent in soil.

Bioaccumulation

Not Bioaccumulative (Not B). Based on low measured bioconcentration factors (BCF) in fish, evidence of biotransformation, and low potential for metabolites to bioaccumulate, galaxolide and musk 89 are categorised as Not Bioaccumulative.

Toxicity

Toxic (T). Based on available acute ecotoxicity values below 1 mg/L and evidence of chronic toxicity (ecotoxicity values below 0.1 mg/L), galaxolide and musk 89 are categorised as Toxic.

Environmental risk characterisation

Based on the PEC and PNEC values determined above, the following Risk Quotients (RQ = PEC ÷ PNEC) have been calculated for release of galaxolide into rivers, soil and sediment:

Compartment	PEC	PNEC	RQ
River	2.0 µg/L	6.8 µg/L	0.29
Soil	0.11 mg/kg dw	0.31 mg/kg dw	0.35
Sediment	0.38 mg/kg dw	1.58 mg/kg dw	0.24

For rivers, an RQ less than 1 indicates that galaxolide is not expected to pose a high risk to the environment based on estimated emissions, as environmental concentrations are below levels likely to cause harmful effects. The RQ considering the worst-case PEC of 4.6 µg/L is 0.68, indicating that galaxolide is not expected to pose a high risk to the environment even at worst-case concentrations in the freshwater aquatic compartment.

For soil, an RQ less than 1 indicates that galaxolide is not expected to pose a high risk to the environment based on estimated emissions, as environmental concentrations are below levels likely to cause harmful effects. The RQ considering the worst-case PEC of 5.5 mg/kg dw is 17.7. This value is calculated using the highest recorded concentration of galaxolide in biosolids in an international study, and concentrations of these magnitudes are unlikely to occur in Australia. However, this worst-case scenario indicates that galaxolide could pose a high risk to the environment if severely contaminated biosolids are applied to agricultural soils in Australia.

For sediment, an RQ less than 1 indicates that galaxolide is not expected to pose a high risk to the environment based on estimated emissions, as environmental concentrations are below levels likely to cause harmful effects. The RQ considering the worst-case PEC of 2.20 mg/kg dw is 1.4. This PEC is the highest recorded concentration of galaxolide in sediment in an international study, from a heavily contaminated urban river in Berlin, Germany. Concentrations of these magnitudes are unlikely to occur in Australia. However, an RQ above 1 indicates that galaxolide could pose a high risk to the environment at worst-case concentrations in sediment.

Marine aquatic organisms may be more sensitive to galaxolide than freshwater organisms of the same trophic level, though there are fewer studies available. However, emissions of galaxolide to the marine environment are unlikely to be a concern where discharge occurs into well-mixed marine waters.

Musk 89 is expected to have similar hazard characteristics, but much lower environmental exposures, to galaxolide. Given the determination that current releases of galaxolide are unlikely to be a concern, the much lower release volumes anticipated for musk 89 mean that this chemical is also unlikely to be a concern. Therefore, it is not expected to pose a high risk to the environment in water, sediment or soil.

Uncertainty

This evaluation was conducted based on a set of information that may be incomplete or limited in scope. Some relatively common data limitations can be addressed through use of conservative assumptions (OECD, 2019) or quantitative adjustments such as assessment factors (OECD, 1995). Others must be addressed qualitatively, or on a case-by-case basis (OECD, 2019).

The most consequential areas of uncertainty for this evaluation are:

- The identity, environmental fate and effects of recalcitrant degradants of galaxolide are unknown. If information becomes available in the future to indicate that these degradants may have persistent, bioaccumulative and toxic (PBT) characteristics, the PBT categorisation of galaxolide may also change.
- There are no domestic monitoring data for galaxolide in the sediment or soil compartments. Measured international concentrations in these compartments indicate that galaxolide may be present at concentrations exceeding the level of concern in heavily contaminated soils and sediments. The risk profile of galaxolide may change should monitoring data become available to indicate that galaxolide is present in Australian soils or sediments at levels above the levels of concern.
- This evaluation focuses on the discrete chemical known as galaxolide (CAS No. 1222-05-5), but in practice galaxolide is used as a technical mixture containing minor structural isomers in concentrations up to 30%. Information was not readily available on whether the test substance used in standard tests (physical and chemical properties, biodegradation, bioaccumulation and toxicity) was pure galaxolide, or the technical mixture containing significant amounts of the structural isomers of galaxolide. It is also uncertain how each of these materials would impact the results of each test, though it is assumed that the properties of the structural isomers are closely modelled by galaxolide. The risk profile of galaxolide may change if information becomes available to indicate that the structural isomers of galaxolide present as impurities in the technical mixture have more hazardous properties than galaxolide.

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