Celestolide and related polycyclic musks: Environment tier II assessment

10 March 2017

CAS Registry Numbers: 13171-00-1, 15323-35-0, 68140-48-7, 103272-81-7, 185438-11-3, 6682-59-3

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies’ umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit: www.nicnas.gov.au.

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Acronyms & Abbreviations

Grouping Rationale

This Tier II assessment considers the environmental risks associated with the industrial uses of celestolide (CAS RN 13171-00-1) and five other similar organic substances that have a common bicyclic acetylindane ring system. The risk assessment of these substances has been conducted as a group because they all have known or potential applications as synthetic polycyclic musks.

Synthetic musks, which include nitromusks, polycyclic musks and macrocyclic musks, are primarily used as ingredients in fragrance mixtures. Polycyclic musks are widely used, and various international studies have identified the bicyclic acetyltetralin musk, tonalide (CAS RNs 21145-77-7 and 1506-02-1), and/or the tricyclic musk, galaxolide (CAS RN 1222-05-5), in almost all household products with added fragrances that have been sampled (e.g.(Reiner and Kannan, 2006)). The environmental risks resulting from the use of tonalide as a fragrance ingredient in Australia have been assessed as part of the IMAP Environment Tier II Assessment for Tonalide and Related Polycyclic Musks (NICNAS, 2016).

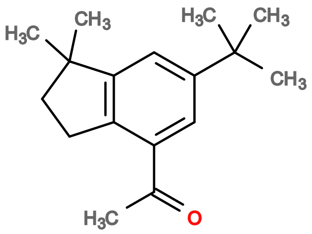
Fragrance ingredients are ubiquitous components of numerous classes of formulated products including cosmetics, personal hygiene products, and various household cleaning agents. These products are released into sewers nationwide as a normal part of their use pattern. Consequently, the use of polycyclic musks in these products has significant potential to result in environmental exposure through a common pathway involving release of the chemicals in the treated effluents and biosolids produced by sewage treatment plants (STPs).

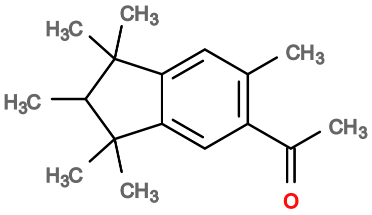
The Tier I assessment of celestolide indicated that it was potentially a persistent, bioaccumulative and toxic (PBT) substance and, therefore, of high environmental concern. This Tier II assessment includes further refinement of the risk characterisation for celestolide and a more in-depth assessment of the available environmental hazard and exposure information for this substance. This assessment also includes a review of the available environmental hazard and exposure information for five closely related acetylindanes which are listed on the Inventory and therefore available for industrial uses, including as fragrance ingredients, in Australia.

Chemical Identity

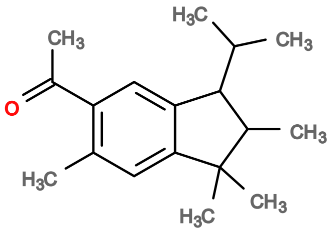
There are two pairs of structural isomers in this group. The first pair is celestolide and phantolide (CAS RN 15323-35-0), which differ in the type and position of substituents (including the acetyl group) on both rings of the indane ring system. The second pair is comprised of the isomers identified by CAS RNs 103272-81-7 and 185438-11-3, which have different relative positions of the acetyl and methyl groups on the benzene ring of the common indane ring system.

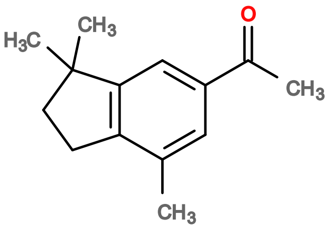
Although both phantolide and traseolide (CAS RN 68140-48-7) have stereoisomeric forms, the stereochemistry of these two chemicals is not specified in their respective Chemical Abstracts Service chemical names as listed on the Inventory. The technical form of traseolide used industrially is understood to be composed of two enantiomers, where the five-membered ring is exclusively in the *trans* configuration (Wang, et al., 2014). No information was identified to indicate that technical phantolide is other than a racemic (equal) mixture of the two enantiomers of this chemical.

CAS RN	13171-00-1
Chemical Name	Ethanone, 1-[6-(1,1-dimethylethyl)-2,3-dihydro-1,1-dimethyl-1H-inden-4-yl]-
Synonyms	celestolide crysolide ADBI
Structural Formula	
Molecular Formula	$C_{17}H_{24}O$
Molecular Weight (g/mol)	244.37
SMILES	C(C)(=O)c1c2c(C(C)(C)CC2)cc(C(C)(C)C)c1

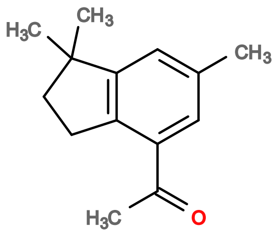
CAS RN	15323-35-0
Chemical Name	Ethanone, 1-(2,3-dihydro-1,1,2,3,3,6-hexamethyl-1H-inden-5-yl)-
Synonyms	phantolide AHMI (or AHDI)
Structural Formula	
Molecular Formula	$C_{17}H_{24}O$
Molecular Weight (g/mol)	244.37
SMILES	O=C(c(c(cc(c1C(C2C)(C)C)C2(C)C)C)c1)C

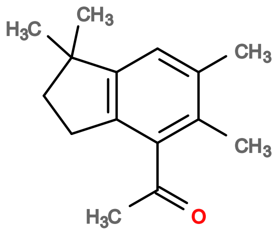
CAS RN	68140-48-7
Chemical Name	Ethanone, 1-[2,3-dihydro-1,1,2,6-tetramethyl-3-(1-methylethyl)-1H-inden-5-yl]-
Synonyms	traseolide (or traesolide) ATII (or AITI)
Structural Formula	

	
Molecular Formula	$C_{18}H_{26}O$
Molecular Weight (g/mol)	258.41
SMILES	O=C(c(c(cc(c1C(C2C)C(C)C)C2(C)C)C)c1)C

CAS RN	103272-81-7
Chemical Name	Ketone, methyl 3,3,7-trimethyl-5-indanyl
Synonyms	ethanone, 1-(2,3-dihydro-3,3,7-trimethyl-1H-inden-5-yl)-
Structural Formula	
Molecular Formula	$C_{14}H_{18}O$
Molecular Weight (g/mol)	202.30
SMILES	C1(C)(C)c2c(c(C)cc(C(C)=O)c2)CC1

CAS RN	185438-11-3

Chemical Name	Ethanone, 1-(2,3-dihydro-1,1,6-trimethyl-1H-inden-4-yl)-
Synonyms	ketone, methyl 1,1,6-trimethyl-4-indanyl
Structural Formula	
Molecular Formula	$C_{14}H_{18}O$
Molecular Weight (g/mol)	202.30
SMILES	C(C)(=O)c1c2c(C(C)(C)CC2)cc(C)c1

CAS RN	6682-59-3
Chemical Name	Ethanone, 1-(2,3-dihydro-1,1,5,6-tetramethyl-1H-inden-4-yl)-
Synonyms	ketone, methyl 1,1,5,6-tetramethyl-4-indanyl
Structural Formula	
Molecular Formula	$C_{15}H_{20}O$
Molecular Weight (g/mol)	216.33

SMILES	c12C(C)(C)CCc1c(C(=O)C)c(C)c(C)c2

Physical and Chemical Properties

There are very few measured values available for the physical and chemical properties of the chemicals in this group. Therefore, the values for key chemical properties such as octanol-water partition coefficient (K_{ow}), water solubility and vapour pressure were all calculated using standard quantitative structure-property relationships (QSPR) (US EPA, 2008):

Chemical	celestolide	ketone, methyl 1,1,6-trimethyl-4-indanyl
Physical Form	solid	solid
Melting Point	77.2–77.9°C (exp.)	80.6°C (calc.)
Boiling Point	319.1°C (calc.)	290.3°C (calc.)
Vapour Pressure	0.03 Pa (calc.)	0.128 Pa (calc.)
Water Solubility	1.15 mg/L (calc.)	15.85 mg/L (calc.)
Ionisable in the Environment?	no	no
log K_{ow}	5.93 (calc.)	4.57 (calc.)

Based on calculated values, all of the chemicals in this group are lipophilic substances, and they are slightly to moderately soluble in water. As expected for fragrance chemicals, they are all estimated to be moderately volatile.

Import, Manufacture and Use

Australia

Based on information in the public domain, celestolide, phantolide and traseolide are available for use in Australia as fragrance ingredients (Australian Botanical Products, 2017).

No specific Australian use, import, or manufacturing information has been identified for the other chemicals in this group.

International

Polycyclic musks have a musky odour and are used as ingredients in fragrance formulations due to their strong odour and fixative properties, and act to bind to other substances and to surfaces such as fabrics and skin (Reiner and Kannan, 2006). Fragrance formulations containing polycyclic musks are typically used in detergents, fabric softeners and conditioners, cleaning agents, furniture polish, and air fresheners. They are also used in personal care products such as soaps, shampoos, perfumes and deodorants (Reiner and Kannan, 2006; Rimkus, 1999).

Polycyclic musks were developed in the 1950s and they gradually replaced nitromusks (Mogensen, et al., 2004; Peters, 2005). Macrocyclic musks are gradually replacing polycyclic musks (Peters, 2005).

Chemicals in this group are used in smaller volumes than some other polycyclic musks, such as galaxolide and tonalide (HERA, 2004; Mogensen, et al., 2004). The total use volume of celestolide, phantolide and traseolide in Europe was 30 tonnes in 2000 (HERA, 2004). In Denmark, the total use volume for these three chemicals was less than 16 kg per annum (Mogensen, et al., 2004).

Celestolide, phantolide and traseolide are listed on the IFRA Transparency List, which identifies chemicals used as fragrances by member companies (IFRA, 2017). The remaining chemicals in this group are not listed.

There is also some indication that celestolide is used as a flavouring agent (EFSA, 2008). However, use of the chemical as a food additive is beyond the scope of this assessment, as such use is not considered an industrial use under the *Industrial Chemicals (Notification and Assessment) Act 1989*.

No international use, import, or manufacturing information has been identified for the remaining chemicals in this group.

Environmental Regulatory Status

Australia

The use of the chemicals in this group is not subject to any specific national environmental regulations.

United Nations

None of the chemicals in this group are currently identified as a Persistent Organic Pollutant (UNEP, 2001), ozone depleting substance (UNEP, 1987), or hazardous substance for the purpose of international trade (UNEP & FAO, 1998).

OECD

The chemicals in this group have not been sponsored for assessment under CoCAP (OECD, 2013).

Canada

The chemicals in this group are not listed under Schedule 1 (the Toxic Substances List) of the *Canadian Environmental Protection Act 1999* (CEPA 1999) (Government of Canada, 2016).

Two substances in this group are listed on the Canadian Domestic Substances List (DSL) (Environment Canada, 2013). Celestolide was categorised as not Persistent (not P), Bioaccumulative (B) and not Inherently Toxic to the Environment (not iT_E)

by Environment Canada during the categorisation of the DSL. Traseolide was categorised as not P, B and iT_E, and was prioritised for further assessment under the Chemicals Management Plan (CMP) (Government of Canada, 2013).

Phantolide was deleted from the DSL in 2009 and added to the Non-Domestic Substances List (NDSL) (Government of Canada, 2009a; b).

European Union

Four substances in this group (celestolide, phantolide, traseolide and ketone, methyl 1,1,5,6-tetramethyl-4-indanyl) were pre-registered under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) legislation (ECHA, 2015).

None of the chemicals in this group have undergone the full registration process.

United States of America

Three substances in this group (celestolide, phantolide and traseolide) are listed on the inventory of chemicals manufactured or processed in the USA, as published under the *Toxic Substances Control Act 1976* (TSCA) (US EPA, 2015).

Environmental Exposure

Three members of this group (celestolide, phantolide and traseolide) are known to be used as fragrance ingredients internationally, and all three have been identified in some perfumes (Peters, 2005). These chemicals could also be used as fragrance ingredients in other consumer products, such as other cosmetics, air fresheners, personal hygiene products, and various household cleaning agents. The formulation of such products on the Australian market is assumed to not differ significantly from those found internationally. Therefore, celestolide, phantolide and traseolide are all expected to have some potential to be found in household and commercial products available for use in Australia.

Chemicals used in cosmetics, personal hygiene and cleaning products are typically released to sewers in wastewater as a normal part of their use pattern. Depending on degradation and partitioning processes of chemicals in sewage treatment plants, 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 through application of biosolids to agricultural land. Based on the high lipophilicity of celestolide, phantolide and traseolide, and taking into account standard removal efficiencies, up to 85% of the total quantity of these chemicals entering a typical STP may be removed by adsorption to sludge, which may be applied to land as biosolids (Struijs, 1996). Hence, emissions of all three chemicals to both environmental surface waters and soils are considered as part of this assessment.

The assumed use of traseolide and phantolide as components of fragrance ingredients in consumer products available in Australia is supported by a recent domestic environmental monitoring study which identified these chemicals in untreated Sydney wastewater (Wang and Khan, 2014). No domestic environmental monitoring data for the remaining three chemicals in this group were identified for this assessment. However, if used as fragrance ingredients these chemicals are also expected to be released to the environment by pathways that are similar to those identified for celestolide, phantolide and traseolide.

Environmental Fate

Partitioning

The chemicals in this group are expected to partition between water and sediment when released to surface waters, and they are expected to have low mobility in soil.

Celestolide is a neutral organic chemical that is expected to be only slightly soluble in water and moderately volatile (US EPA, 2008). The calculated Henry’s Law constant for celestolide is 3.22 Pa-m^3/mol (at 25°C) (US EPA, 2008), which indicates that celestolide is expected to be moderately volatile from water and moist soil. Celestolide is also a highly lipophilic chemical, which typically indicates that it will have low mobility in soil.

Calculations with a standard multimedia partitioning (fugacity) model assuming equal and continuous distributions to air, water and soil compartments (Level III approach) predict that celestolide will mainly partition to the soil compartment (81.9%), with minor partitioning to the water compartment (12.8%) and the sediment compartment (4.65%) (US EPA, 2008). However, with sole release to the aquatic compartment, it is predicted that celestolide will predominantly partition to water (73.1%) with significant partitioning to the sediment compartment also expected (26.5%) (US EPA, 2008).

The other chemicals in this group also partition between water and sediment when released solely to the aquatic compartment (59–94% to water and 6–40% to sediment). As for celestolide, the estimated partitioning of the other chemicals in this group to air and soil is low in this scenario (< 0.2%).

Degradation

The chemicals in this group are expected to undergo slow biodegradation in water and soil.

Celestolide has been found to be not inherently biodegradable in a study conducted according to OECD Test Guideline 302C, undergoing less than 1% biodegradation in 28 days (OSPAR Commission, 2000). A low level of mineralisation was observed for phantolide in a two-phase closed bottle test conducted according to ISO 107018. Some data are available to indicate that phantolide undergoes primary biodegradation to more polar metabolites in soil (OSPAR Commission, 2000).

No studies on the biodegradation of other chemicals in this group were identified for this assessment. All of the chemicals in this group are predicted to be not readily biodegradable according to standard quantitative structure-activity relationships (QSAR) (US EPA, 2008).

Some partitioning to the air compartment is expected for all chemicals in this group based on their volatility and their function as fragrances in consumer products. Based on the results of calculations with standard QSPRs, all of the chemicals in this group are predicted to undergo rapid photo-oxidation by hydroxyl radicals in the troposphere (half-life < 2 days) (US EPA, 2008). This prediction is supported by the findings of studies on the gas phase reactions of hydroxyl radicals with structurally related fragrance chemicals such as galaxolide which show that the measured and estimated rates of reaction are within a factor of 1.3 to 1.5 (ECB, 2008).

Bioaccumulation

The bioaccumulation potential of the chemicals in this group is uncertain.

No experimental bioaccumulation data are available for the chemicals in this group. The measured bioconcentration factors (BCF) in fish for other lipophilic polycyclic musks, such as galaxolide and tonalide, are lower than BCF values calculated based on log K_{OW} values (Dietrich and Hitzfeld, 2004). Experimental studies have demonstrated that galaxolide and tonalide are metabolised in fish to more polar compounds, which are more easily excreted than the parent chemicals. The standard quantitative structure-bioaccumulation relationships appear to underestimate the biotransformation of these polycyclic musks, which can lead to an overestimation of the bioaccumulation hazard in fish.

The chemicals in this group have estimated octanol-water partition coefficients that exceed the domestic categorisation threshold for bioaccumulation hazards in aquatic organisms (log $K_{OW} \geq 4.2$). The calculated BCF values in upper trophic level fish for all chemicals in this group also exceed the domestic categorisation threshold for bioaccumulation (BCF ≥ 2000 L/kg) when the effects of biotransformation are excluded. However, when the predicted rate of biotransformation in fish for each chemical is included, the calculated BCF values are all below the categorisation threshold (223–1320 L/kg) (US EPA, 2008).

Based on this analysis, it is concluded that all of the chemicals in this group have some potential to bioconcentrate in fish, although the magnitude of the bioaccumulation hazard is currently uncertain.

Celestolide, phantolide and traseolide have been detected in human adipose tissue and breast milk (Mogensen, et al., 2004). However, it is noted that humans may have direct exposure to these chemicals from the use of cosmetics and personal hygiene products, and these findings are therefore not necessarily indicative of transfer of these chemicals through the food chain.

Transport

Chemicals in this group have the potential to travel long distances through the atmosphere.

Environmental monitoring has identified celestolide, phantolide and traseolide in pristine environmental areas, including remote alpine lakes and glaciers in Switzerland (Bogdal, et al., 2009; Schmid, et al., 2007). As these environments do not typically receive direct anthropogenic outputs, these findings suggest the potential input of polycyclic musks to these sites by wet and gaseous deposition after transport of the chemicals through the atmosphere from distant emission sources (Schmid, et al., 2007).

Predicted Environmental Concentration (PEC)

The predicted environmental concentrations for celestolide, phantolide and traseolide are based on domestic and international monitoring data for these chemicals in wastewater effluents and biosolids. Based on international monitoring data, the maximum concentration of celestolide in Australian effluents is estimated to be 0.17 µg/L.

The predicted environmental concentration for celestolide in surface waters can be estimated assuming an annual introduction volume of 100 tonnes per annum as outlined in the IMAP Framework, and assuming no biodegradation in STPs for recalcitrant chemicals. If standard exposure modelling for the release of chemicals to surface waters in STP effluents is used for this scenario, the concentration of celestolide in rivers is estimated to be 8.5 µg/L (EPHC, 2009; NICNAS, 2013; Struijs, 1996).

However, international monitoring data indicate this may overestimate typical environmental concentrations. Celestolide, phantolide and traseolide are frequently found in sewage sludge, but only rarely in treated effluents as they are mostly removed in STPs (Törneman, 2008). At an advanced wastewater treatment and water recycling plant in Sydney, the average influent concentrations of phantolide and traseolide (0.002 and 0.005 µg/L) were significantly lower than the measured levels of galaxolide and tonalide (2.55 and 0.30 µg/L), and well below the estimated concentrations assuming default introduction volumes. This suggests that domestic use of polycyclic musks in fragrance ingredients is dominated by galaxolide and tonalide, as occurs internationally. Phantolide and traseolide were not detected in the final treated effluent which was subjected to both reverse osmosis and disinfection steps before re-use (Wang and Khan, 2014). It should be noted that musk concentrations measured in effluent after advanced treatment processes may not be representative of concentrations in treated effluents nationwide.

Studies conducted in Europe and America found celestolide in STP effluents at concentrations between 0.01 and 0.43 µg/L, where the reported 90th percentile concentration in Germany was 0.17 µg/L (Brändli, 2002; Chase, et al., 2012; OSPAR Commission, 2004). This 90th percentile value has been used as the maximum concentration of celestolide in Australian effluents for the purposes of risk characterisation in this assessment. Reported concentrations of phantolide and traseolide in these European and American effluents were 0.006–0.12 µg/L (90th percentile concentration is 0.36 µg/L) and < 0.01–0.79 µg/L (90th percentile concentration is 0.62 µg/L), respectively (Brändli, 2002; OSPAR Commission, 2004).

Celestolide, phantolide and traseolide levels measured in biosolids from multiple wastewater treatment plants around the world are 0.07–1100 µg/kg, 0.41–1800 µg/kg, and up to 1000 µg/kg, respectively (Harrison, et al., 2006; Langdon, et al., 2010; Mogensen, et al., 2004). The concentration of celestolide in soil following a single application of biosolids to land has been estimated to be in the range 0.002 to 33.8 µg/kg (Langdon, et al., 2010).

If the remaining three chemicals in this group are used as fragrance ingredients domestically, they are only expected to be used in small volumes resulting in limited environmental emissions. The environmental concentrations of the three remaining chemicals in this group have, therefore, not been estimated.

Environmental Effects

Effects on Aquatic Life

Chemicals in this group are expected to cause toxic effects at low concentrations in aquatic organisms across multiple trophic levels.

Acute toxicity

The following measured median lethal concentration (LC50) and median effective concentration (EC50) values for model organisms across three trophic levels were retrieved from the scientific and regulatory literature for (a) celestolide, (b) phantolide, and (c) traseolide (Brausch and Rand, 2011; OSPAR Commission, 2000; Yamauchia, et al., 2008):

Taxon	Endpoint	Method
Fish	(a) 96 h LC50 = 1.97 mg/L	Experimental *Oryzias latipes* (Japanese rice fish) Test substance was dissolved in 0.1% DMSO
	(b) 96 h LC50 = 1.22 mg/L	Experimental *Oryzias latipes* Test substance was dissolved in 0.1% DMSO
	(c) 96 h LC50 = 0.95 mg/L	Experimental *Oryzias latipes* Test substance was dissolved in 0.1% DMSO
Invertebrates	(a) 48 h LC50 > 2.0 mg/L	Experimental *Acartia tonsa* (saltwater copepod)
	(b) 48 h EC50 = 0.33 mg/L	Experimental *Daphnia magna* (Water flea)
	(c) 48 h EC50 = 0.42 mg/L	Experimental *Daphnia magna*

Taxon	Endpoint	Method
Algae	(b) 72 h EC50 = 0.2 mg/L	Experimental *Selenastrum capricornutum* (Green algae) Growth rate inhibition

The potential for celestolide and traseolide to cause toxic effects in some organisms through inhibition of multixenobiotic resistance transporters has been discussed (Luckenbach and Epel, 2005). However, insufficient data are currently available to evaluate the potential for this effect to cause adverse outcomes in organisms exposed to polycyclic musks in the environment.

No measured aquatic toxicity data for the remaining three chemicals in this group were identified. The acute aquatic toxicity of these three chemicals was instead estimated using standard QSARs (US EPA, 2012). All three chemicals are categorised as neutral organic chemicals with a non-polar narcosis (or baseline) mode of toxic action in aquatic organisms. The predicted 96 h LC50 values for acute toxicity of all three chemicals to fish is below 1 mg/L (0.29–0.83 mg/L). The estimated acute toxicity values for daphnids are also below 1 mg/L for all three chemicals, indicating that these chemicals are toxic at low concentrations to aquatic organisms from multiple trophic levels. These predictions are consistent with the measured toxicity values for the other three members of this group.

Chronic toxicity

The following measured no-observed-effect concentrations (NOEC) for model organisms across two trophic levels were retrieved from the scientific and regulatory literature for (a) celestolide and (b) phantolide (Breitholtz, et al., 2003; OSPAR Commission, 2000):

Taxon	Endpoint	Method
Invertebrates	(a) 7–8 d NOEC = 0.03 mg/L	Experimental *Nitocra spinipes* (brackish water copepod) Semi static. Acetone was used as a solvent control.
Algae	(b) 72 h NOEC = 0.044 mg/L	Experimental *Selenastrum capricornutum* Growth rate inhibition

Effects on Terrestrial Life

There are no suitable data available to evaluate the effects of the chemicals in this group on terrestrial life.

Predicted No-Effect Concentration (PNEC)

The euryhaline invertebrate, *Nitocra spinipes*, was found to be sensitive to chronic exposures to celestolide. The NOEC derived from the effects of celestolide on this species in a 7–8 day exposure study was used to derive an aquatic PNEC of 0.3 µg/L, after applying an assessment factor of 100. The maximum assessment factor of 100 was selected to account for the limited available chronic aquatic toxicity data for the chemical and uncertainties regarding the bioaccumulation potential of celestolide in aquatic organisms (EPHC, 2009).

Categorisation of Environmental Hazard

The categorisation of the environmental hazards of ethanone, 1-[6-(1,1-dimethylethyl)-2,3-dihydro-1,1-dimethyl-1H-inden-4-yl]- (celestolide); ethanone, 1-(2,3-dihydro-1,1,2,3,3,6-hexamethyl-1H-inden-5-yl)- (phantolide); ethanone, 1-[2,3-dihydro-1,1,2,6-tetramethyl-3-(1-methylethyl)-1H-inden-5-yl]- (traseolide); ketone, methyl 3,3,7-trimethyl-5-indanyl; ethanone, 1-(2,3-dihydro-1,1,6-trimethyl-1H-inden-4-yl)-; and ethanone, 1-(2,3-dihydro-1,1,5,6-tetramethyl-1H-inden-4-yl)- according to domestic environmental hazard thresholds is presented below (EPHC, 2009; NICNAS, 2013):

Persistence

Persistent (P). Based on the results of biodegradation studies conducted on celestolide and phantolide, and considering the results of quantitative structure-property modelling of biodegradability, all chemicals in this group are categorised as Persistent.

Bioaccumulation

Uncertain (Uncertain B). There is currently insufficient information to conclude whether bioconcentration of the chemicals in this group in aquatic organisms exceeds the domestic categorisation threshold. The bioaccumulation potential of the chemicals in this group is therefore categorised as Uncertain.

Toxicity

Toxic (T). Based on measured chronic toxicity values below 0.1 mg/L for both celestolide and phantolide, and acute toxicity values below 1.0 mg/L for both phantolide and traseolide, all three chemicals are categorised as Toxic. The remaining chemicals have modelled acute toxicity end-points below 1 mg/L and are, therefore, also categorised as Toxic.

Summary

All chemicals in this group are categorised as:

- P
- Uncertain B
- T

Risk Characterisation

The below risk quotient (RQ = PEC ÷ PNEC) for the riverine compartment has been calculated based on the PEC and PNEC values determined for celestolide:

PEC (µg/L)	PNEC (µg/L)	RQ

PEC (µg/L)	PNEC (µg/L)	RQ
0.17	0.3	0.57

An RQ of less than 1 indicates that industrial uses of celestolide are not expected to pose an unreasonable risk to the environment, as environmental concentrations are below the levels likely to cause harmful effects. Therefore, industrial use of the chemical is not expected to pose an unreasonable risk to the aquatic environment.

The risk quotients for release of phantolide and traseolide to river water have not been calculated as the concentrations in treated wastewater are expected to be below the level of concern. This assessment is based on the measured concentrations of both chemicals in the influent to an advanced wastewater treatment and water recycling plant in Sydney (0.002 µg/L for phantolide and 0.005 µg/L for traseolide), which are less than 3% of the maximum concentration of celestolide that is assumed to occur in treated effluents discharged to surface waters in Australia. It is noted that international studies reported that the concentrations of phantolide and traseolide in STP effluents are comparable to the concentrations of celestolide. This suggests that the environmental concentration used for the aquatic risk characterisation of celestolide in this assessment overestimates the potential for aquatic exposure to this chemical in Australia.

There are currently no suitable soil toxicity data available to estimate the risks to the soil compartment from the application of biosolids containing chemicals in this group. However, it should be noted that the estimated concentrations of chemicals in this group in soil are likely to be significantly lower than those estimated for polycyclic musks that are used in higher volumes, such as tonalide. For example, it is estimated that the maximum concentration of celestolide in soil following application of biosolids to land will be 0.034 mg/kg. This is less than 0.3% of the maximum concentration calculated for tonalide (13 mg/kg), which is persistent in soil and known to have some toxicity to soil organisms (Langdon, et al., 2010; NICNAS, 2016).

Key Findings

The chemicals in this group are synthetic polycyclic musks. Three of the chemicals in this group, celestolide, phantolide and traseolide, are known to have current industrial uses as fragrance ingredients in personal care products such as perfumes. Based on international use data, these three chemicals are used in relatively small volumes compared to other polycyclic musks.

Two of the chemicals in this group, phantolide and traseolide, have been measured in low concentrations in wastewater entering a water treatment plant in Australia. No measurements of the concentration of celestolide in wastewater streams or surface waters in Australia were identified for this assessment. Based on concentrations measured internationally, celestolide is not considered likely to be released to surface waters in Australia at concentrations that exceed the level of concern. All three chemicals are considered likely to be present as contaminants in biosolids based on extensive international monitoring data. However, the concentrations of these chemicals occurring in agricultural soils following the application of biosolids are not considered to be of concern.

The chemicals in this group are categorised as persistent (P) and toxic (T) according to domestic environmental hazard criteria. The chemicals in this group have the potential to bioconcentrate in aquatic organisms, but the magnitude of the bioaccumulation hazard is currently uncertain (Uncertain B).

Further assessment of these chemicals under the IMAP Framework may be required if information becomes available to indicate that chemicals in this group have high bioaccumulation potential, or if measured environmental concentrations exceed the level of concern.

Recommendations

No further assessment is currently required.

Environmental Hazard Classification

In addition to the categorisation of environmental hazards according to domestic environmental thresholds presented above, the classification of the environmental hazards of (a) ethanone, 1-[6-(1,1-dimethylethyl)-2,3-dihydro-1,1-dimethyl-1H-inden-4-yl]- (celestolide); (b) ethanone, 1-(2,3-dihydro-1,1,2,3,3,6-hexamethyl-1H-inden-5-yl)- (phantolide); and (c) ethanone, 1-[2,3-dihydro-1,1,2,6-tetramethyl-3-(1-methylethyl)-1H-inden-5-yl]- (traseolide) according to the third edition of the United Nations' Globally Harmonised System of Classification and Labelling of Chemicals (GHS) is presented below (UNECE, 2009a):

Hazard	GHS Classification (Code)	Hazard Statement
Acute Aquatic	(a) Category 2 (H401)	Toxic to aquatic life
	(b) and (c) Category 1 (H400)	Very toxic to aquatic life
Chronic Aquatic	(a), (b) and (c) Category 1 (H410)	Very toxic to aquatic life with long lasting effects

The classification of the acute aquatic hazards posed by celestolide, phantolide and traseolide was performed based on the acute ecotoxicity data presented in this assessment.

The long-term aquatic hazards of celestolide and phantolide were classified based on the available chronic aquatic toxicity data taking into account the non-rapid degradation of this chemical in aquatic ecosystems (UNECE, 2009a). The classification of long-term aquatic hazard of traseolide was performed using the GHS method for substances for which adequate chronic toxicity data are not available, noting the non-rapid degradability of the chemical and its estimated log K_{ow} value which is greater than 4 (UNECE, 2009b).

The remaining chemicals in this group are not classified for this assessment.

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