Australian Government
Department of Health
Australian Industrial Chemicals Introduction Scheme

OTNE and constituent isomers

Evaluation statement

14 January 2022

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AICIS evaluation statement

Subject of the evaluation

Isomers of octahydro tetramethyl naphthalenyl ethanone (OTNE)

Chemicals in this evaluation

Name	CAS Numbers
Ethanone, 1-(1,2,3,4,5,6,7,8-octahydro-2,3,8,8-tetramethyl-2-naphthalenyl)-	54464-57-2
Ethanone, 1-(1,2,3,4,5,6,7,8-octahydro-2,3,5,5-tetramethyl-2-naphthalenyl)-	54464-59-4
Ethanone, 1-(1,2,3,5,6,7,8,8a-octahydro-2,3,8,8-tetramethyl-2-naphthalenyl)-	68155-66-8
Ethanone, 1-(1,2,3,4,6,7,8,8a-octahydro-2,3,8,8-tetramethyl-2-naphthalenyl)-	68155-67-9

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 use of octahydro tetramethyl naphthalenyl ethanone (OTNE), a technical mixture principally comprising 4 isomers (CAS Nos. 54464-57-2, 54464-59-4, 68155-66-8, 68155-67-9) that is used as a synthetic fragrance. The 4 isomers are listed on the Australian Inventory of Industrial Chemicals (the Inventory). This chemical mixture has been assessed for its risk to the environment according to the following parameters:

- default domestic introduction volume 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.

Summary of evaluation

Summary of introduction, use and end use

OTNE is a common fragrance ingredient in a variety of cosmetic and consumer use products worldwide and has a global use volume in the thousands of tonnes per year. There are no specific domestic introduction volume data available for OTNE, but fine perfumes that are known to contain the chemical are available for sale in Australia.

OTNE is used in the following products according to reported international use data:

- Apparel and footwear care products
- Plastic and polymer products
- Air freshener products
- Automotive care products
- Cleaning and furniture care products
- Laundry and dishwashing products
- Personal care products

Environment

Summary of environmental hazards

According to domestic environmental hazard thresholds and based on the available data the chemicals are:

- Not Persistent (not P)
- Not Bioaccumulative (not B)
- Toxic (T)

Environmental hazard classification

The chemicals satisfy the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) for environmental hazards as follows (UNECE, 2017). This does not consider classification of physical hazards and health hazards:

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (acute / short-term)	Aquatic Acute 2	H401: Toxic to aquatic life
Hazardous to the aquatic environment (long-term)	Aquatic Chronic 2	H411: Toxic to aquatic life with long lasting effects

Summary of environmental risk

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

The OTNE isomers are toxic, have low bioaccumulation potential, and are not persistent in the environment.

Based on measured international concentrations in STP effluent, surface waters, sediment and biosolids, OTNE isomers are expected to be present in Australian river, sediment and soil compartments at concentrations below the level of concern.

Conclusions

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

Supporting information

Rationale

This evaluation considers environmental risks associated with the industrial uses of four closely related isomers that are collectively known as octahydro tetramethyl naphthalenyl ethanone (OTNE). The chemicals share a common octahydronaphthalene core substituted with an acetyl group and four methyl groups. The evaluation of these substances has been conducted as a group because all are constituents of technical OTNE with known applications as polycyclic fragrance chemicals.

The name 'OTNE' is often used synonymously with the most abundant component of the mixture, the beta isomer (CAS No. 54464-57-2). The other chemicals evaluated in this group are minor components: the minor isomer (CAS No. 54464-59-4), gamma isomer (CAS No. 68155-66-8) and alpha isomer (CAS No. 68155-67-9).

OTNE was developed as a synthetic amber fragrance, with a woody, floral scent reminiscent of ambergris (Hall and Sanders, 1975a). OTNE is a high production volume chemical internationally and is commonly found in fine perfumes, personal care and household products. 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 OTNE 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 OTNE.

Environmental risks resulting from the use of other synthetic fragrance ingredients in Australia have previously been assessed under the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework established by the former Scheme, 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

OTNE is a mixture of structural isomers that contain an octahydronaphthalene core with one site of unsaturation in the ring, tetramethyl substitution and an acetyl substituent. The isomers differ in the position of the double bond and substituent functional groups. The isomers in OTNE mixtures that are listed on the Australian Inventory of Industrial Chemicals (Inventory) are the: beta isomer (CAS No. 54464-57-2), gamma isomer (CAS No. 68155-66-8), alpha isomer (CAS No. 68155-67-9), and minor isomer (CAS No. 54464-59-4) (OTNE Consortium, 2020).

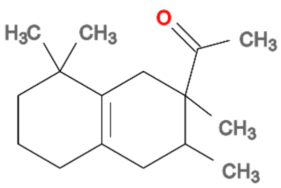
The structure of the beta isomer and the CAS No. 54464-57-2 are commonly used to identify both the beta isomer alone and the technical mixture of all OTNE isomers.

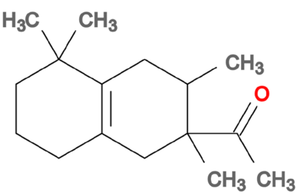
OTNE technical mixtures are synthesised in a two-step procedure. In the first step a Diels-Alder cycloaddition of myrcene and 3-methyl-3-penten-2-one gives a cyclohexene product.

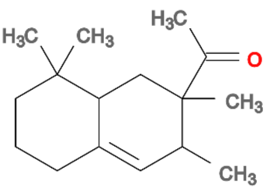
Use of a Lewis acid regioselectively positions the acetyl group in the 4-position with respect to the isohexenyl chain. In the second step a Brønsted acid-catalysed cyclisation closes the naphthalene ring (Hall and Sanders, 1975a). Different isomers are formed due to imperfect regioselectivity in the first step (leading to the beta and the minor isomer) and the acid-catalysed alkene migration after the second step (leading to the gamma and the alpha isomer). OTNE technical mixtures synthesised by different industrial producers vary in isomer ratio depending on the specific reaction conditions used (Armanino, et al., 2020; Fráter and Schröder, 2007; Stepanyuk and Kirschning, 2019). Typical OTNE mixtures consist of 30–65% beta isomer, 10–33% gamma isomer, 8–20% alpha isomer, and 0–5% minor isomer (OTNE Consortium, 2020).

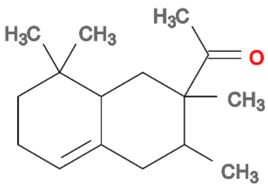
The OTNE isomers listed on the Inventory do not have defined stereochemistry and are assumed to be mixtures of stereoisomers. As the Diels-Alder reaction is a stereospecific *syn*-addition, it is expected that the methyl groups in the resulting isomers will have a *cis* configuration if (3*E*)-3-methyl-3-penten-2-one is used as a substrate. The identified isomers of OTNE are structurally analogous and have the same functional use, so their physico-chemical properties and behaviour in the environment are also expected to be similar.

Structural and stereoisomers that are not listed on the Inventory but may be present in OTNE mixtures include: the enantiomeric mixture of (2*RS*,3*RS*)-beta stereoisomers (CAS RN 59056-94-9), Iso E Super Plus (CAS No. 140194-26-9), (+)-Iso E Super Plus (1R,2R,8aS, CAS No. 356088-90-9), and Georgywood (CAS No. 185429-83-8). (+)-Iso E Super Plus is in the technical mixture in concentrations of 2.5–14.9% and is responsible for the characteristic scent of OTNE (Armanino, et al., 2020). Georgywood is another isomer with a potent scent that differs from other OTNE components in that it can be synthesised as a single chemical on the industrial scale (Armanino, et al., 2020; Fráter and Schröder, 2007; Stepanyuk and Kirschning, 2019):

CAS No.	54464-57-2
Chemical Name	ethanone, 1-(1,2,3,4,5,6,7,8-octahydro-2,3,8,8-tetramethyl-2-naphthalenyl)-
Synonyms	naphthalene, 2-acetyl-1,2,3,4,5,6,7,8-octahydro-2,3,8,8-tetramethyl- OTNE OTNE beta isomer Iso E Super 2-acetyloctahydro-2,3,8,8-tetramethylnaphthalene Isocyclemone E Boisvelone Orbitone Iso Velvetone Patchouli ethanone Anthamber Amberonne Amber Fleur Velvetone Timbersilk
Structural Formula	
Molecular Formula	$C_{16}H_{26}O$
Molecular Weight (g/mol)	234.38
SMILES	O=C(C(C(CC(=C1C(CC2)(C)C)C2)C)(C1)C)C
Chemical Description	-

CAS No.	54464-59-4
Chemical Name	ethanone, 1-(1,2,3,4,5,6,7,8-octahydro-2,3,5,5-tetramethyl-2-naphthalenyl)-
Synonyms	OTNE minor isomer
Structural Formula	
Molecular Formula	$C_{16}H_{26}O$
Molecular Weight (g/mol)	234.38
SMILES	CC1CC2=C(CCCC2(C)C)CC1(C)C(=O)C
Chemical Description	-

CAS No.	68155-66-8
Chemical Name	ethanone, 1-(1,2,3,5,6,7,8,8a-octahydro-2,3,8,8-tetramethyl-2-naphthalenyl)-
Synonyms	OTNE gamma isomer Iso Gamma
Structural Formula	
Molecular Formula	$C_{16}H_{26}O$
Molecular Weight (g/mol)	234.38
SMILES	CC1C=C2CCCC(C2CC1(C)C(=O)C)(C)C
Chemical Description	-

CAS No.	68155-67-9
Chemical Name	ethanone, 1-(1,2,3,4,6,7,8,8a-octahydro-2,3,8,8-tetramethyl-2-naphthalenyl)-
Synonyms	OTNE alpha isomer Iso Alpha
Structural Formula	
Molecular Formula	$C_{16}H_{26}O$
Molecular Weight (g/mol)	234.38
SMILES	CC1CC2=CCCC(C2CC1(C)C(=O)C)(C)C
Chemical Description	-

Relevant physical and chemical properties

Measured physical and chemical property data for technical OTNE (only comprising the beta, gamma and alpha isomers) were retrieved from the registration dossier submitted under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) legislation in the European Union (EU) (REACH, 2021).The Henry's Law Constant was calculated from measured values for water solubility and vapour pressure (US EPA, 2017a).There are no measured values available for the physical and chemical properties of the minor isomer. Values were calculated using standard quantitative structure-property relationships (QSPR) (US EPA, 2017a):

Chemical	Beta, gamma and alpha isomers	Minor isomer
Physical Form	Liquid	Solid
Melting Point	-20°C (exp.)	85.8°C (calc.)
Boiling Point	290.4°C (exp.)	296.8°C (calc.)
Vapour Pressure	0.233 Pa at 23°C (exp.)	0.147 Pa (calc.)
Water Solubility	2.68 mg/L at 20°C (exp.)	1.08 mg/L (calc.)
Henry's Law Constant	2.04 Pa·m^3/mol (calc.)	4.76 Pa·m^3/mol (calc.)
Ionisable in the Environment?	No	No
pKa	N/A	N/A
log K_{ow}	5.65 at 30°C (exp.)	5.18 (calc.)

Introduction and use

Australia

No specific Australian import or manufacturing information has been identified for technical OTNE.

Based on information in the public domain, OTNE is readily available for use in Australia as a fragrance ingredient.

International

Available information indicates that OTNE is used at high volumes as a fragrance ingredient in a range of products worldwide.

OTNE is used in the EU in the range of 1000–10 000 tonnes per year (t/year) (REACH, 2021). In the United States of America (USA) OTNE is listed as a high production volume chemical (US EPA, 2021), with an annual use volume of 4536–22 680 t/year. Constituent isomers are reported separately; the minor isomer has an annual use volume of 24 t/year, the gamma isomer has an annual use volume of 454 – 9072 t/year, and the alpha isomer has an annual use volume of <454 t/year (US EPA, 2016). In Canada the Domestic Substances List (DSL) quantity range is 1–1000 t/year (ECCC, 2021). In the Nordic countries, the average annual use volume over a five-year period from 2015–2019 was 22.72 t/year (SPIN, 2019b). The gamma isomer was reported separately, and has an average annual use volume over the same five-year period of 6.56 t/year (SPIN, 2019a).

OTNE isomers (beta, gamma and alpha) are listed on the International Fragrance Association (IFRA) transparency list, which identifies chemicals used as fragrances by member companies (IFRA, 2021). OTNE is used as a fragrance component in perfumes; a survey conducted by the Research Institute for Fragrance Materials (RIFM) found that OTNE is used in fine fragrances in a concentration of 4.5% in the final formulation (95th percentile)

(OTNE Consortium, 2020). Many fine perfumes contain OTNE, for example: *Molecule 01* and *Escentric 01* by Escentric Molecules (100 and 65% of the fragrance component, respectively) (Escentric Molecules, 2021; Schön, 2008); *Poivre Samarcande* by Hermès (71%); *Feminite du Bois* by Shisheido (43%); *Dolce Vita* and *Fahrenheit* by Christian Dior (25% each); and *Trésor* by Lancôme (18%) (Nussbaumer, et al., 1999; Stepanyuk and Kirschning, 2019).

Other products that contain OTNE include air freshener products in a concentration of 21% (95^{th} percentile), lipstick, deodorant, cosmetics, creams, lotions and soap, all in a concentration of <1% (95^{th} percentile concentration) (OTNE Consortium, 2020). OTNE is also found in other personal care products (shaving cream, shampoo, conditioner, hair removal products), cleaning products (laundry detergent, fabric softener, dish soap, surface cleaners, polishes and waxes) and automotive care products (leather care products, upholstery cleaner and deodorisers) (CPID, 2021; ECHA, 2021a).

OTNE may have site-limited uses in production of polyurethane foam and plastics (McDermott, et al., 1995) and industrial uses in tobacco products (Hall and Sanders, 1975b).

Georgywood is listed on the IFRA transparency list (IFRA, 2021) and is used as a fragrance ingredient in fine perfumes, such as 27 87 Perfume's 'Genetic Bliss' (Armanino, et al., 2020).

OTNE has non-industrial use in biocidal products (disinfectants and pest control) (ECHA, 2021a). Use of the chemical as a pesticide additive is beyond the scope of this assessment.

Existing Australian regulatory controls

Environment

The use of OTNE is not subject to any specific national environmental regulations.

International regulatory status

United Nations

OTNE isomers 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).

European Union

In 2017, OTNE (reaction mass of beta, alpha and gamma isomers) was included in ECHA's Community Rolling Action Plan (CoRAP) indicating that it will be evaluated due to its suspected PBT characteristics, wide dispersive release, and exposure to the environment. Conclusions have yet to be released (ECHA, 2021b).

United States of America

All OTNE isomers in this group were identified and prioritised for assessment in the 2014 update to the Toxic Substances Control Act (TSCA) Work Plan (US EPA, 2014).

Two of the isomers (the beta and minor isomers) were categorised as potential PBT chemicals in the 2014 TSCA Work Plan, and; therefore, candidates of a rule under Section 6(h) of the Toxic Substances Control Act that enables expedited regulatory action before a risk evaluation is carried out. Under this section, stakeholders had the opportunity to request a risk evaluation by the US EPA in order to avoid regulatory action. The two OTNE isomers were nominated by a consortium of manufacturers by the required deadline (US EPA, 2019).

The US EPA received an official request to conduct a risk evaluation of the OTNE technical mixture in December, 2020 (OTNE Consortium, 2020). The risk evaluation had not been published at the time of writing.

Asia

The OTNE technical mixture (comprising beta, gamma and alpha isomers) has been classified as a Priority Assessment Chemical Substance (PACS) under Japan's Chemical Substances Control Law, indicating that these chemicals have been prioritised for assessment (METI, 2021).

Other

The International Fragrance Association (IFRA) has restricted the use of the OTNE technical mixture in finished products to concentrations of 0.0093%–20% depending on the product category (IFRA, 2020).

Environmental exposure

OTNE isomers are expected to be found in household and commercial products available for use in Australia. OTNE 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 surveys have measured OTNE in air freshener products, cosmetics and personal care products (OTNE Consortium, 2020) and this chemical is an ingredient in fine perfumes (Nussbaumer, et al., 1999; Stepanyuk and Kirschning, 2019). Consumer product information supports this use profile and also indicates that OTNE is used in household cleaners and automotive care products (CPID, 2021; ECHA, 2021a). A portion of chemicals used in air freshener products and fine perfumes will be released to the air compartment, and 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 OTNE to environmental surface waters, sediment, soil and air are considered as part of this evaluation.

Environmental fate

Partitioning

OTNE isomers partition to air, water, sediment and soil when released to the environment.

OTNE isomers are neutral organic chemicals that are expected to be slightly soluble in water and moderately volatile. Measured and calculated Henry's Law constants (2.04 and 4.76 Pa·m^3/mol, respectively) indicate that these chemicals will be moderately volatile from water and moist soil. The isomers are lipophilic and have a calculated soil adsorption coefficient of log K_{OC} = 3.52. This indicates that they will have slight mobility in soil but will preferentially adsorb to phases in the environment with high organic carbon content (including sediment and soil) (REACH, 2021; US EPA, 2017a).

The majority of OTNE is expected to be released to the water compartment as a result of its use. Fugacity calculations (Level III approach) assuming sole release to the aquatic environment predict that the OTNE isomers will primarily remain in water (80.7–80.9%) and partition to sediment (19.0–19.2%), with negligible partitioning to soil and air (each < 0.1%) (US EPA, 2017a).

OTNE isomers 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 OTNE isomers will predominately be found in soil (99.9%) (US EPA, 2017a).

Degradation

OTNE isomers are not expected to be persistent in the environment.

According to a recent ready biodegradability test conducted according to OECD TG 301F and provided to AICIS, Department of Health, OTNE isomers are readily biodegradable in water with 96% biodegradation measured by biological oxygen demand (BOD) over 28 days (Unpublished report, 2021). This test used a non-standard test substance concentration of 19 mg/L and inoculum sampled from a STP receiving primarily domestic sewage. A toxicity control was also conducted, reaching 86% degradation by day 28. The test substance is; therefore, not considered toxic to the inoculum as the toxicity control reached >25% degradation by day 14. The validity criteria of the test guideline were satisfied, with degradation of the sodium benzoate reference compound reaching 93% by day 8, confirming the suitability of the conditions and inoculum. The maximum difference in degradation rate between the two test substance replicates was less than 20%. The inoculum blank reached a maximum of 21.1 mg O_2/L by the end of the test, within the acceptable range.

Previous tests conducted according to standard test guidelines indicated that OTNE isomers were not readily biodegradable in water (REACH, 2021). The outcomes of these tests suggest that the test substance concentration or inoculum sampling location may have an impact on the test results. In an OECD TG 301C ready biodegradation test with 30 mg/L test substance concentration, the mean biodegradation was 0% based on BOD. This test used a mixed inoculum sampled from domestic and industrial STPs, as well as river surface waters. In an OECD TG 301F ready biodegradability test using 100 mg/L test substance concentration and inoculum sampled from an STP receiving domestic sewage, no biodegradation was observed even after the test duration was extended to 42 days. Lastly, in an OECD TG 302C inherent biodegradability test using 30 mg/L test substance and a high domestic STP sludge inoculum concentration of 100 mg/L, no biodegradation was observed over 28 days (REACH, 2021).

In a separate die-away study in river water inoculated with activated sludge (method equivalent to OECD TG 314), the primary half-life of a technical mixture of OTNE was < 1 day at 20°C (REACH, 2021). Relatively low mineralisation (10% over 28 days) was observed in this test, suggesting that some of the metabolites of OTNE isomers have a longer residence time in the environment than the parent chemicals.

OTNE isomers are expected to degrade in sediment with a primary degradation half-life of 9.5 days and an ultimate biodegradation half-life of approximately 10 weeks based on a study equivalent to OECD TG 308. After 8 weeks less than 1% of the isomers comprising OTNE remained, and in the same period 40% had mineralised to CO_2 (0.8% per day after a 7-day lag period). The remaining material was accounted for by polar degradants (REACH, 2021). The half-life of the chemicals is within domestic categorisation thresholds for persistence (EPHC, 2009).

OTNE isomers have an expected primary half-life of 4.2 and 6 days in biosolid-amended and agricultural soil, respectively, and an ultimate half-life of 5–6 weeks according to a study equivalent to OECD TG 307. Mineralisation was observed at a rate of 1.4–1.8% per day after a 7 day lag period, placing OTNE within domestic categorisation thresholds for persistence (EPHC, 2009; REACH, 2021).

Calculations from standard quantitative structure-activity relationships (QSARs) predict that OTNE isomers will degrade in air following reaction with hydroxyl radicals during daylight with a half-life of 1.4 hours, and nitrate radicals during the night with a half-life of 2 minutes (Aschmann, et al., 2001). OTNE in biosolid-amended soil (loamy sand) undergoes photodegradation under artificial sunlight with a half-life of 7.1 days (Ozaki, et al., 2011).

Bioaccumulation

OTNE isomers have low potential to bioaccumulate in aquatic life, and uncertain potential to bioaccumulate in benthic and soil organisms. Metabolites of OTNE isomers are more polar than the parent chemicals 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). A study conducted according to OECD TG 305 reported a BCF of 391 litres per kilogram (L/kg) wet weight (wwt) in *Lepomis macrochirus* (bluegill sunfish, normalised to 5% lipid weight). OTNE was rapidly depurated, with a DT50 of 1.2 days (REACH, 2021).

Limited data are available to evaluate the bioaccumulation potential of OTNE isomer metabolites. However, identified metabolites are more polar than the parent isomers and are expected to be rapidly cleared by aquatic organisms. During the principal OECD TG 305 bioconcentration study with *L. macrochirus* the total radioactive residue (TRR) of radiolabelled OTNE was tracked, enabling the study of metabolites formed over the experiment (REACH, 2021). OTNE isomers were readily metabolised by the fish, and after the exposure period of 21 days a study of TRR in fish viscera revealed 7-10 chemical components. Of this, 30-35% was accounted for by two polar metabolites and 50% by the parent compounds. Metabolites were detected in surrounding water, showing that they are excreted by the fish.

The beta isomer of OTNE was predicted to have a BCF of 285 L/kg wwt in a study using in vitro data (rate of metabolism in trout liver cells) to refine BCF estimates for the whole fish. Assays were conducted using five isomers in the OTNE technical mixture, but only the major beta isomer could be identified from included percentage composition data. The beta isomer had slower clearance in vitro than the minor isomers: 0.33 compared to 0.64–0.71 mL/h/mg protein, respectively. The beta isomer was predicted to have a BCF of 285 L/kg wwt (compared to 238-243 L/kg wwt for minor isomers) (Laue, et al., 2014).

Benthic organisms are exposed to OTNE isomers in sediment, and soil-dwelling organisms are exposed to OTNE when biosolids containing the chemical are applied to agricultural soil. However, the risk of bioaccumulation is uncertain due to limited evidence.

Environmental transport

OTNE isomers are not expected to undergo long range transport based on their short half-lives in air.

OTNE isomers have a short predicted atmospheric lifetime of 1.2 hours during daylight hours and 2 minutes at night, suggesting atmospheric transport is unlikely (Aschmann, et al., 2001). There are no environmental monitoring studies available that have detected OTNE isomers in pristine environmental areas that do not receive anthropogenic inputs, but the widespread use of OTNE and the suspected long range transport of fragrance chemicals with similar use patterns (NICNAS, 2016; 2017) suggest this could be possible for OTNE isomers.

Predicted environmental concentration (PEC)

The concentration of OTNE in Australian river water is estimated to be 1.58 micrograms per litre (µg/L), based on data of STP effluent concentrations from an extensive international study, with a worst-case concentration of 17.8 µg/L. Reasonable worst-case concentrations of OTNE in domestic sediments and soil are predicted to be 0.87 and 0.34 mg/kg dry weight (dw), respectively, based on data from international monitoring studies.

No domestic environmental monitoring studies are available, but OTNE has been measured internationally in STP influent and effluent, surface waters, sediment and biosolids.

OTNE has been measured in concentrations of 3.25–21.5 µg/L in STP influent in international studies (Bester, et al., 2008b; Klaschka, et al., 2013; Simonich, et al., 2000). Effluent concentrations range from 0.02–17.8 µg/L, but average values are more commonly <3.5 µg/L and depend on the level of STP treatment (Klaschka, et al., 2013; OTNE Consortium, 2020; Pintado-Herrera, et al., 2014; Simonich, et al., 2002; Terzić, et al., 2008). For example, a study at an STP in Germany measured effluent concentrations of 1.42–1.84 µg/L after primary treatment and 0.11–0.33 µg/L after secondary treatment (Simonich, et al., 2000). An extensive study across 44 STPs in the USA reported a 90th percentile OTNE concentration in wastewater effluent of 1.58 µg/L (McDonough, et al., 2017) and this value has been used as the estimate OTNE surface water concentration in Australia for the purposes of risk characterisation. The maximum concentration of 17.8 µg/L measured in effluent is taken as a worst-case PEC in Australian surface waters. Effluent concentrations of these magnitudes are unlikely to occur in Australia, but this endpoint defines the upper boundary of the PEC upon release of highly contaminated effluents to Australian rivers.

International studies have quantified OTNE in surface waters (rivers, tidal waters, groundwater) in concentrations up to 5.46 µg/L (Pintado-Herrera, et al., 2014), measured in a river downstream of STP effluent. Concentrations in rivers are highly variable on the extent that they are impacted by anthropogenic pollution; a study in Germany measured OTNE concentrations of 0.029–0.039 µg/L in less polluted waterways and 0.019–0.81 µg/L in rivers impacted by sewage sludge (Bester, et al., 2008a; Klaschka, et al., 2013; Schwientek, et al., 2016). Two studies in Spain detected OTNE in the tidal channels and estuaries of an enclosed marine bay in average concentrations of 0.40 and 0.68 µg/L (Pintado-Herrera, et al., 2014; Pintado-Herrera, et al., 2020). OTNE has been detected in groundwater in an average concentration of 0.52 µg/L, as measured from an alluvial aquifer in Spain (Pintado-Herrera, et al., 2020).

After entering the aquatic compartment OTNE accumulates in sediment in concentrations up to 0.87 mg/kg dw, with the highest concentrations detected in an urban canal receiving large quantities of STP effluent (Wishneff, 2012). In contrast, marine sediments contain lower concentrations of OTNE; the chemical was measured in concentrations of 0.003–0.057 mg/kg dw at six sampling sites off the Spanish coast and accounted for 15–45% of all fragrance chemicals detected (Pintado-Herrera, et al., 2016). A value of 0.87 mg/kg dw has been used as a reasonable worst-case concentration of OTNE in Australian sediments for the purposes of risk characterisation.

OTNE adsorbs to biosolids in STPs during processing and has been detected in concentrations of 0.73–212 mg/kg dw internationally, with a 90^{th} percentile concentration of 50.7 mg/kg dw in the USA (Bester, et al., 2008b; DiFrancesco, et al., 2004; McDonough, et al., 2017).

The calculated OTNE concentration in soil amended with biosolids is 0.34 mg/kg dw based on the 90^{th} percentile concentration of OTNE in biosolids in the USA (50.7 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 worst-case concentration of 6.52 mg/kg dw calculated using the maximum measured concentration of OTNE in biosolids (212 mg/kg dw) and maximum biosolids application rates.

OTNE in surface waters can be taken up by aquatic biota, leading to measurable quantities in fish and clams. OTNE has been detected in carp kept for 6-8 months in ponds receiving treated STP wastewater. Concentrations in muscle and liver were <10 – 47 ng/g fresh weight (fw) and 10-510 ng/g fw, respectively (Klaschka, et al., 2013). Maximum concentrations of 69.5 ng/g dw were measured in clams installed in a closed marine bay for one year (Pintado-Herrera, et al., 2020).

Environmental effects

Effects on aquatic life

OTNE isomers are expected to cause toxic effects at low concentrations in aquatic organisms across multiple trophic levels.

OTNE isomers are categorised as non-polar (or baseline) toxicants and are expected to have acute toxic effects largely determined by their potential to partition from water to biological membranes (US EPA, 2017b).

Acute toxicity

The following measured median lethal concentration (LC50) and median effective concentration (EC50) values for model organisms across three trophic levels exposed to OTNE were retrieved from the Registration Dossier for the OTNE under EU REACH legislation (REACH, 2021).

Taxon	Endpoint	Method
Fish	96 h LC50 = 1.3 mg/L	*Lepomis macrochirus* (bluegill sunfish) Semi-static conditions OECD TG 203
Invertebrate	48 h EC50 = 1.38 mg/L	*Daphnia magna* (water flea) Mobility Semi-static conditions OECD TG 202
Algae	72 h EC50 > 2.6 mg/L	*Scenedesmus subspicatus* Growth rate and biomass OECD TG 201

Chronic toxicity

The following measured no-observed-effect concentrations (NOEC) for model organisms across three trophic levels were retrieved from the Registration Dossier for OTNE under EU REACH legislation (REACH, 2021).

Taxon	Endpoint	Method
Fish	30 d NOEC = 0.16 mg/L	*Danio rerio* (zebrafish) Body weight and length Semi-static (0–4 d) and flow-through (4–30 d) OECD TG 210
Invertebrates	21 d NOEC = 0.028 mg/L	*Daphnia magna* Reproduction Flow-through conditions OECD TG 211
Algae	72 h NOEC > 2.6 mg/L	*Scenedesmus subspicatus* Growth rate OECD TG 201

Effects on terrestrial life

These OTNE isomers are not expected to cause toxic effects to terrestrial organisms at low concentrations.

Chronic ecotoxicity values have been obtained for the earthworm *Eisenia foetida* exposed to a technical mixture of OTNE in standard soil with 10% added organic matter (sphagnum peat) in a study conducted according to OECD TG 222 (ISO TG 11268). Adult *E. foetida* exposed to OTNE exhibited 28 day NOECs of 31.6 mg/kg dw (body weight) and 100 mg/kg dw (mortality). An 8 week NOEC of 31.6 mg/kg dw (reproduction) was obtained for worm offspring exposed to OTNE (REACH, 2021).

A mixture of 6 agriculturally relevant plants were exposed to technical OTNE for 14 days, including *Brassica napus* (rapeseed), *Glycine max* (soybean), *Solanum lycopersicum* (tomato), *Cucumis sativus* (cucumber) and *Avena sativa* (common oat). *Allium cepa* (onion) was exposed to the chemical for 21 days. The plants were sown in sandy loam (0.67% organic matter) and OTNE had a 10% effective concentration (EC10) for emergence, growth and phytotoxic effects of 27 mg/kg dw (REACH, 2021).

The impact of a technical mixture of OTNE on soil microorganisms was tested according to OECD TG 216. OTNE was added to soil amended with powdered plant meal (lucerne), and a 28 day NOEC of 100 mg/kg dw (nitrogen transformation: nitrate content and formation rate) was measured (REACH, 2021).

Effects on sediment dwelling life

These OTNE isomers are not expected to cause toxic effects to sediment-dwelling organisms at low concentrations.

The following measured no-observed-effect-concentration (NOEC) values for three model organisms exposed to technical OTNE in sediments were retrieved from the Registration Dossier for the chemical under EU REACH legislation (REACH, 2021). All endpoint values were corrected for standard sediment containing 5% total organic carbon content.

Taxon	Endpoint	Method
Midge	28 d NOEC = 102 mg/kg dw	*Chironomus riparius* (harlequin fly) Survival/ratite midges 2.24% organic content OECD TG 218
Worm	28 d NOEC = 17.1 mg/kg dw	*Lumbriculus variegatus* (blackworm) Reproduction/biomass 2.29% organic content OECD TG 218
Amphipod crustacean	28 d NOEC = 18.4 mg/kg dw	*Hyalella azteca* Survival/biomass 2.33% organic content OECD TG 218

Endocrine effects/activity

No evidence of endocrine effects or activity have been identified for this evaluation.

Predicted no-effect concentration (PNEC)

A freshwater PNEC for OTNE of 2.8 µg/L was derived from the measured invertebrate chronic ecotoxicity endpoint (21 d NOEC = 0.028 mg/L), using an assessment factor of 10. This assessment factor was selected as reliable chronic ecotoxicity data are available over three trophic levels (EPHC, 2009).

A soil PNEC of 1.07 mg/kg dw was derived from the measured earthworm chronic ecotoxicity endpoint (8 week NOEC = 31.6 mg/kg dw). Following the approach used in the EU Risk Assessment Report for the synthetic fragrance Galaxolide, the NOEC for *E. foetida* was first normalised to a soil organic content of 3.4% (ECB, 2008). An assessment factor of 10 was then applied, selected because reliable chronic ecotoxicity data are available over three taxa (EPHC, 2009).

A sediment PNEC of 2.99 mg/kg dw was derived from the measured blackworm chronic ecotoxicity endpoint (28 d NOEC = 17.1 mg/kg dw). Following the approach above, the NOEC for *L. variegatus* was first normalised to a sediment organic content of 4%. An assessment factor of 10 was then applied and was selected because reliable chronic ecotoxicity data are available over three taxa (EPHC, 2009).

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

Not persistent (Not P). Based on standard biodegradability tests that demonstrate ultimate degradation in the aquatic compartment, OTNE isomers are categorised as Not Persistent.

Bioaccumulation

Not Bioaccumulative (Not B). Based on low measured bioconcentration factors (BCF) in fish, and evidence of biotransformation, OTNE isomers are categorised as Not Bioaccumulative.

Toxicity

Toxic (T). Based on evidence of high chronic toxicity (ecotoxicity values below 0.1 mg/L), OTNE isomers 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 OTNE into rivers, soil and sediment:

Compartment	PEC	PNEC	RQ
River	1.58 µg/L	2.8 µg/L	0.57
Soil	0.34 mg/kg dw	1.07 mg/kg dw	0.32
Sediment	0.87 mg/kg dw	2.99 mg/kg dw	0.29

For rivers, an RQ less than 1 indicates that OTNE is not expected to pose a significant risk to the environment based on the estimated emissions, as environmental concentrations are below levels likely to cause harmful effects. The RQ considering the worst-case PEC of 17.8 µg/L is 6.36. This value is calculated using the highest recorded concentration of OTNE in

STP effluent in an international study, and concentrations of these magnitudes are unlikely to occur in Australia. However, the worst-case scenario indicates that OTNE could pose a significant risk to the environment if highly contaminated effluents are released to Australian rivers.

For sediments, an RQ less than 1 indicates that OTNE is not expected to pose a significant risk to the environment based on the estimated emissions, as environmental concentrations are below levels likely to cause harmful effects.

For soil, an RQ less than 1 indicates that OTNE is not expected to pose a significant risk to the environment based on the estimated emissions, as environmental concentrations are below levels likely to cause harmful effects. The RQ considering the worst-case PEC of 6.52 mg/kg dw is 6.09. This value is calculated using the highest recorded concentration of OTNE in biosolids in an international study, and concentrations of these magnitudes are unlikely to occur in Australia. However, the worst-case scenario indicates that OTNE could pose a significant risk to the environment if highly contaminated biosolids are applied to agricultural soils in Australia.

Uncertainty assessment

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:

- There are no domestic monitoring data for OTNE in the river, sediment or soil compartments. Measured international concentrations in the river and soil compartments indicate that OTNE may be present at concentrations exceeding the level of concern in heavily contaminated rivers and soils. There is also no domestic use volume data. The risk profile of OTNE may change should use volume or monitoring data become available to indicate that OTNE is present in Australian surface waters, sediments or soils at levels above the levels of concern.
- The OTNE technical mixture is defined in this evaluation as a mixture of four isomers (beta, minor, alpha and gamma) with proportions that vary within defined ranges (see Chemical identity section). The properties of isomers in the OTNE technical mixture are assumed to be similar, so technical mixtures with different compositions are expected to have similar hazard characteristics. The risk profile of OTNE may change if information becomes available to indicate that mixtures with differing isomer concentrations have significantly different hazard properties.
- There is evidence that the OTNE technical mixture contains additional isomers that are not on the Inventory (Iso E Super Plus, Georgywood). Therefore, their risk to the environment has not been evaluated. It is assumed that the risk characterisation of additional isomers is modelled by the chemicals in this evaluation. The risk profile of OTNE may change if information becomes available to indicate that these chemicals are more hazardous than the evaluated isomers.

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