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

Benzoic acid, 2-hydroxy-, 3,3,5-trimethylcyclohexyl ester (Homosalate)

Evaluation statement

1 October 2024

Draft

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AICIS evaluation statement

Subject of the evaluation

Benzoic acid, 2-hydroxy-, 3,3,5-trimethylcyclohexyl ester (Homosalate)

Chemical in this evaluation

Name	CAS registry number
Benzoic acid, 2-hydroxy-, 3,3,5-trimethylcyclohexyl ester	118-56-9

Reason for the evaluation

Evaluation Selection Analysis indicated a potential human health and environmental risk.

Parameters of evaluation

The chemical is listed on the Australian Inventory of Industrial Chemicals (the Inventory).

This evaluation statement includes an environment and human health risk assessment for all identified industrial uses of benzoic acid, 2-hydroxy-, 3,3,5-trimethylcyclohexyl ester (homosalate). The use of homosalate in therapeutic sunscreens is not assessed in this evaluation.

The risks posed to the environment associated with the industrial uses of homosalate have been assessed according to the following parameters:

- A domestic introduction volume of 159 tonnes per year, based on industry consultation.
- Industrial uses listed in the 'Summary of introduction, use and end use' section.
- Expected emission to sewage treatment plants (STPs) following consumer and commercial use.

Summary of evaluation

Summary of introduction, use and end use

Homosalate has a reported introduction volume in Australia of 159 tonnes per annum (for both therapeutic and industrial uses). Personal care products (cosmetics) containing homosalate including face cream and lip balm have been identified on Australian commercial websites.

Based on international use information, homosalate is used as a UV-filter in secondary sunscreens but may also be used in fragrances due to its scent. The main source of human exposure was identified to be face creams and lip balms (up to 10%).

The chemical also has reported non-industrial use in therapeutic sunscreens.

Human health

Summary of health hazards

The identified health hazards are based on the available data for the chemical.

Based on physicochemical properties the chemical is expected to be readily available following oral exposure, and to a lesser extent following dermal exposure. Based on calculated vapour pressure, inhalation exposure is not expected unless aerosols are formed. The chemical has been detected in human milk and in plasma. The major metabolites are expected to be salicylic acid and 3,3,5-trimethylcyclohexanol although unmetabolised homosalate and other metabolites have been detected in oral and dermal studies in humans.

Based on the available data, the chemical:

- has low acute oral and dermal toxicity
- is not irritating to eyes or skin
- is not considered to be a potent skin sensitiser
- is not considered to have genotoxic potential
- is not expected to be carcinogenic.

Based on the limited available data, homosalate may adversely affect the kidney. In a combined repeated dose toxicity with reproduction and developmental toxicity screening toxicity study in rats (OECD Test Guideline (TG) 422), kidney effects, including increased weight and presence of hyaline droplets were observed in male rats at 60 mg/kg bw/day. There was insufficient information available to conclude that these effects were due to a rat specific mechanism dependent accumulation of α2u-globulin. Therefore, the observed kidney effects were considered relevant to humans and the lowest observed adverse effect level (LOAEL) was considered to be 60 mg/kg bw/day. Other organ effects occurred mainly at doses ≥300 mg/kg bw/day and included an increase in absolute and relative liver weights, decreased thymus weight and a higher incidence of diffuse hypertrophy in the thyroid.

Based on the limited available data, homosalate may affect fertility and development toxicity (reduced fertility index, sperm changes, reduced corpora lutea and higher post-implantation loss) were observed. Only one screening study (OECD TG 422) is available for the chemical. However, rats in this study were exposed to constant lighting instead of a typical light-dark cycle and; therefore, this study cannot be considered to be as conclusive and reliable. The reported no observed adverse effect level (NOAEL) for fertility was reported as 120 mg/kg bw/day based on effects on fertility (post-implantation loss) at doses ≥300 mg/kg bw/day. Due to the low number of pregnant females in the study a NOAEL for development toxicity was not determined. The likely metabolite of homosalate, salicylic acid, is associated with adverse effects on development. However, in the absence of further information, it is unclear to what degree the salicylic acid metabolite may contribute to developmental toxicity from homosalate.

Current available data do not provide sufficient evidence of an adverse effect of the chemical from an endocrine mode of action. The chemical was shown to interact with oestrogen, androgen and progesterone receptors in some in vitro assays, although at potencies several magnitudes lower than endogenously produced hormones.

For further details of the health hazard information see **Supporting Information**.

Hazard classifications relevant for worker health and safety

The chemical does not satisfy the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant for work health and safety.

Summary of health risk

Public

Based on the available use information, the public may be exposed to the chemical:

- at concentrations up to 10%
- by direct application of the chemical to the skin, hair or lips
- by inhaling aerosols.

This chemical has the potential to cause adverse systemic effects. To estimate risk, margins of exposure were calculated for various use scenarios including:

- individual and aggregate exposure to 5 products that contribute significantly to the overall daily systemic exposure at a concentration of 10%
- aggregate exposure to the most frequently used products (face cream and lip products) at a concentration of 10%
- aggregate exposure to the most frequently used products (face cream and lip products) at a reduced concentration.

The calculated margins of exposure (MOE) were <100 for face cream, hand cream and combined use of face cream and lip balm at concentrations of 10% indicating that the chemicals may pose a risk of adverse systemic effects. For combined use of face cream and lip balm a concentration of 4.35% resulted in an MOE of 100.

Given the identified health hazard the evidence indicates that there is a risk to the public that requires management (see **Proposed means of managing risk**). The risk could be managed by listing the chemical in the *Poison Standard - Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP).*

Workers

Based on its hazard profile, the chemical is unlikely to pose a risk to workers. However, given the potential for adverse effects on the kidney and uncertainty relating to developmental toxicity, information in this report should be used by a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) to determine the appropriate controls.

Environment

Summary of environmental hazard characteristics

Based on the information presented in this evaluation statement and according to the environmental hazard thresholds stated in the Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals, the chemical is:

- not persistent (Not P)
- not bioaccumulative (Not B)
- toxic (T).

Environmental hazard classification

This chemical satisfies 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 evaluation does not consider classification of physical hazards.

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (long-term)	Aquatic Chronic 1	H410: Very toxic to aquatic life with long lasting effects

Summary of environmental risk

The chemical is expected to be mainly released into the environment via the sewer. For surface waters, sediment and soil, a risk quotient (RQ) less than 1 indicates that the chemical is not expected to pose a significant risk to the environment based on estimated diffuse emissions, as environmental concentrations are below levels likely to cause harmful effects.

Homosalate may also be released directly to recreational waters by washing off the bodies of recreational water users while in use. However, this exposure route is expected to be particularly relevant to therapeutic sunscreens. International monitoring data suggests that some recreational water bodies, such as beaches and reefs that are near heavily populated areas or are visited by high numbers of tourists, may be subject to localised, transient elevated concentrations of homosalate. Conservative worst case treatment of these locations would result in RQs >1, indicating the presence of transient risks. However, there are no acute effects expected at the limit of water solubility, the chemical is rapidly degradable and will be dispersed within the water bodies, thus limiting the potential environmental risks. In the absence of Australian specific monitoring data linking environmental concentrations to different classes of products, there is insufficient evidence to characterise the risk to the environment at these locations from either the industrial or the therapeutic uses of homosalate.

The chemical has been categorised under domestic thresholds as not persistent, not bioaccumulative and toxic. The chemical has also been found to interact with the human and test animal endocrine system in several studies, but only at concentrations that far exceed concentrations that are likely to occur in the environment.

Proposed means for managing risk

Public health

Recommendation to Department of Health and Aged Care

It is recommended that the delegate of the Secretary for Poisons Scheduling lists the chemical in the *Poisons Standard* (the SUSMP).

It is recommended that to manage the potential risk associated with the use of the chemical that the entry:

- restricts the concentrations of the chemical in cosmetic products.

Consideration should be given to the following:

- the likely use of the chemical in face creams and lip products in Australia
- exposure to the chemical may damage the kidney
- EU has restricted the chemical to face products only at a maximum concentration of 7.34%; however, this does not consider use in lip products.
- for combined use of face cream and lip balm a concentration of 4.35% resulted in a MOE of 100
- The chemical is also used in therapeutic sunscreens.

Workers

Information relating to safe introduction and use

The information in this statement should be used by a person conducting a business or undertaking at a workplace (such as an employer) to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.

Recommended control measures that could be implemented to manage the risk arising from dermal and inhalation exposure to these chemicals include, but are not limited to:

- minimising manual processes and work tasks through automating processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Measures required to eliminate or manage risk arising from storing, handling and using these hazardous chemicals depend on the physical form and the manner in which the chemicals are used.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk.

Model codes of practice, available from the SWA website, provide information on how to manage the risks of hazardous chemicals in the workplace, prepare an SDS and label containers of hazardous chemicals. Your Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

Conclusions

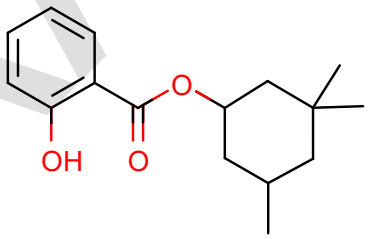
The Executive Director proposes to be satisfied that the identified risks to human health and the environment from the introduction and use of the industrial chemical can be managed.

Note:

1. Obligations to report additional information about hazards under *Section 100* of the *Industrial Chemicals Act 2019* apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Chemical identity

CAS number	118-56-9
CAS name	Benzoic acid, 2-hydroxy-, 3,3,5-trimethylcyclohexyl ester
Molecular formula	$C_{16}H_{22}O_3$
Associated names	Homosalate 3,3,5-Trimethylcyclohexyl salicylate Heliophan Homomenthyl salicylate Salicylic acid, 3,3,5-trimethylcyclohexyl ester Salicylic acid, *m*-homomenthyl ester
Molecular weight (g/mol)	262.34
SMILES (canonical)	O=C(OC1CC(C)CC(C)(C)C1)C=2C=CC=CC2O
Structural formula	

Additional chemical identity information

The chemical is a mixture of 4 isomers, the 2 diastereomers are commonly abbreviated to *cis*-homosalate and *trans*-homosalate. The ratio of diastereomers are dependent on the manufacturing method and have been reported at 40:60 and approx. 90:10 (*cis:trans*) (Ebert et al. 2022).

Relevant physical and chemical properties

Experimental (exp.) and calculated (calc.) values are taken from the registration dossier for homosalate submitted under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) legislation in the European Union (EU) (REACH n.d.-a). While the K_{OC} has been calculated by the MCI method in EPISuite (US EPA 2017a) and the pKa has been calculated by Chemaxon in QSAR Toolbox (LMC 2021):

Physical form	Liquid
Melting point	< -20 °C (exp.)
Boiling point	295.1 °C (exp.)
Vapour pressure	0.015 Pa (exp.)
Water solubility	0.091 mg/L at 20 °C (exp.)
Henry's law constant	43.2 Pa·m^3/mol (calc.)
Ionisable in the environment?	No
pKa	9.72 (calc.)
log K_{ow}	6.27 at 25 °C (exp.)
K_{oc}	6,778 L/kg (calc.)

Introduction and use

Australia

High volumes of homosalate are used internationally for a variety of industrial and therapeutic uses. An Australian voluntary call for information from industry identified that homosalate is commonly used in both cosmetics, which are regulated under the *Industrial Chemicals Act (2019),* and therapeutic sunscreens, which are regulated under the *Therapeutic Goods Act (1989)*. Sunscreen products that are considered to be industrial uses are defined in under the Therapeutic Goods (Excluded Goods) Determination 2018 (TGA 2018). These include the following products that contain sunscreen:

- products applied to the lips (such as lipsticks and lip balms)
- tinted bases and foundations (including liquids, pastes and powders)
- moisturising skin care products
- sunbathing skin care products.

Limitations relating to sun protection factor (SPF), product type, ingredient schedule entry in the SUSMP and pack size apply.

The chemical has reported frequent use in therapeutic sunscreens (O'Malley 2020).

Approximately 159 tonnes of homosalate are being introduced annually (for both therapeutic and industrial uses). The call for information also identified use concentrations of 4-15% with the highest concentrations of homosalate being present in therapeutic sunscreens.

Personal care products (cosmetics) containing homosalate including face cream and lip balm have been identified on Australian commercial websites.

The chemical has reported frequent use in therapeutic sunscreens (O'Malley 2020).

International

The chemical has reported cosmetic uses in a range of products including:

- face cream
- foundation
- lip balm
- body wash
- shampoo
- hand cream
- concealer
- tanning products
- massage products
- perfume/ eau de toilette
- sun oil.

Homosalate is primarily used as an active ingredient in personal care products where it functions as a UV-filter. Based on international data the personal care products that are most likely to contain homosalate are face cream and lip balm (Danish EPA 2015; INCI beauty n.d.; Government of Canada 2020; De Lima Associates n.d.; EWG n.d.). According to notifications under the Canadian Cosmetic Regulations, homosalate is found in face moisturisers, massage products, fragrance products, makeup (non-permanent), bath products, shampoos, and tanning products. Homosalate was imported into Canada in quantities of 1,000,000 to 1,100,000 kgs, respectively, during the 2011 reporting year (Government of Canada 2020). According to the Environmental Working Group (EWG) Skin Deep database, the majority of products containing the chemical are recreational and daily use sunscreens which are likely to be therapeutic sunscreens in Australia. According to the database the chemical is also used in colour correcting cream, lip balm, fragrance for women, body spray, foundation and facial suncare.

Use of whole-body leave-on products (tanning products, massage products and sun oil) are not expected to have frequent (everyday) use patterns.

In an industry survey performed by the Danish Environmental Protection Agency from October 2013 to August 2015, homosalate was found in 27 out of 291 products. Of these, the majority were likely to be used therapeutic sunscreens (18). However, homosalate was also reported to be used in 4 face creams, 2 day creams, 2 lip balms, 1 makeup and 1 foundation product.

The chemical is listed on the International Fragrance Association (IFRA) Transparency List (IFRA n.d.).

Reported concentrations in personal care products included 10% in face creams, 5% in

anti-wrinkle cream and 3% in face moisturiser (De Lima Associates n.d.; Special Chem n.d.) The chemical also has reported use in women's fragrances with typical use concentrations of 0.1–5% (Perfumers World n.d.).

Existing Australian regulatory controls

Public

The chemical has restrictions for its non-industrial use in therapeutic sunscreens and are listed in Therapeutic Goods (Permissible ingredients) Determination (No.2) 2024, Schedule 1- Specified permissible ingredients and requirements applying to these ingredients when contained in a medicine.

Homosalate:

- For use as an active ingredient only in sunscreens for dermal application.
- For use as an excipient only in topical medicines for dermal application.
- Not to be included in medicines intended for use in the eye.
- The concentration in the medicine must not be more than 15%.

Workers

The chemical is not listed on the HCIS (SWA n.d.).

No exposure standards are available for the chemical in Australia (SWA n.d.).

Environment

The reported industrial use of homosalate is not subject to any specific national environmental regulations.

International regulatory status

Canada

Based on the Draft screening assessment – Salicylates group, the Government of Canada is considering:

- Communicating measures to reduce exposures to homosalate from certain cosmetics by describing homosalate as prohibited or restricted ingredients on the Health Canada Cosmetic Ingredient Hotlist.
- Further risk mitigation for homosalate in certain non-prescription drugs under the *Foods and drugs Act* (1985) (Government of Canada 1985).

European Union

The chemical is listed in entry 3 of Annex VI of the EU Cosmetic Regulation (EC) No. 1223/2009 – List of substances which cosmetic products must not contain except subject to the restrictions laid down. The chemical is permitted in ready for use cosmetic products as a UV filter with a maximum concentration of 10%. From the 1st of January 2025 homosalate will

only be permitted in face products with the exception of propellent spray products with a maximum concentration of 7.34% (EC n.d.).

New Zealand

The chemical is listed in the New Zealand Cosmetic Products Group Standard – Schedule 8 List of UV filters which cosmetic products may contain. The maximum authorised concentration in finished cosmetic products is 10% (NZ EPA 2024).

United States of America

Under the US Food and Drug Administration (FDA) Federal Food, Drug, and Cosmetic Act Code of Federal Regulations Title 21, the maximum authorised concentration of the chemical is 15% for sunscreen drug products for over the counter human use (FDA n.d.-a).

Asia

The chemical is restricted under a group entry in the Japan Ministry of Health and Welfare's Standards for Cosmetics (Ministry of Health and Welfare Notification No.331 of 2000). The entry in "Appendix 4: The ingredients restricted in all types of cosmetics" states that total concentration of homomenthyl salicylate (homosalate) in cosmetics has a concentration limit of 10% (Ministry of Health and Welfare Japan 2000).

The chemical is listed in ASEAN Cosmetic Directive Annex VII – List of permitted UV filters which cosmetic products may contain. The maximum authorised concentration in finished products is 10% (ASEAN 2019).

Human exposure

Public

As homosalate is used in a wide range of personal care products (see **Introduction and use**), there is expected to be significant public exposure to the chemical. Oral exposure to the chemical is expected from lip balms. Depending on the type of product, dermal contact with personal care products can be limited to specific areas on the body such as the eye region, face, hands, nails, or feet, or it can be more extensive, covering large areas of the trunk as well as the face. The duration of exposure for various products may differ substantially; for rinse-off products such as soaps or shampoos, exposure might only be for a few minutes, although some residual product can remain, whereas for leave-on products, exposure could last for several hours.

AICIS exposure estimate

The public exposure to homosalate in adults was estimated for scenarios relating to its use in leave-on personal care products. In this exposure assessment, the reasonable worst case approach is used, in which estimates are based on worst-case, but plausible, exposure scenarios.

The oral and dermal exposure to the chemical was calculated as an internal dose which is proportional to the use volumes, product retention factors (reflecting proportions of product remaining on the skin during normal use) and the dermal absorption of homosalate. For the exposure assessment, the use amounts were determined using values previously

established by the SCCS (SCCS 2023a). An absorption value of 5.3% were used for dermal exposure (see **Toxicokinetics**). For lip products 100% oral absorption was assumed. A lifetime average adult body weight (BW) of 60 kg was used for the calculations. This exposure assessment (see **Table 1**) is based on the 5 products that contribute significantly to the overall daily systemic exposure (rinse-off products have been excluded).

Exposure to the chemical was calculated as an internal dose which is proportional to the use volumes, product retention factors (reflecting proportions of product remaining on the skin during normal use) and the dermal absorption of the chemical.

Table 1 – Daily systemic exposure to homosalate from 5 cosmetic products based on the currently maximum allowed concentration in EU.

Type of product	Amount (mg/day)	C (%)	RF (unitless)	A (%)	Daily systemic exposure (mg/kg bw/day)
Face cream	1540	10	1	5.3	0.136
Fine Fragrances	750	10	1	5.3	0.066
Hand cream	2160	10	1	5.3	0.191
Lipstick, lip balm	57	10	1	100	0.095
Liquid foundation	510	10	1	5.3	0.045
Total	**5017**				**0.533**

Daily systemic exposure = (Amount × C × RF × A)/BW

(C = chemical concentration; RF = retention factor; A = oral or dermal absorption; BW = body weight)

Exposure estimates from other international agencies

The Scientific Committee on Consumer Safety (SCCS) previously conducted a risk assessment to determine whether aggregate exposure to homosalate from a range of cosmetic and personal care products was safe at the current EU concentration limits (see **International restrictions**).

The SCCS has conducted exposure assessments to determine the aggregate exposure to the chemical from a range of cosmetic and personal care products at the current EU concentration limits (see **International restrictions**). For dermal absorption of the test substance, a value of 5.3% was used. The calculated aggregate daily systemic exposure to the chemical from oral, dermal and inhalation exposure for lipstick, face cream and hand cream was 0.327 mg/kg bw/day (SCCS 2020).

The systemic exposure doses (SED) for dermal and inhalation exposure were calculated for face creams and face pump spray containing 7.34% homosalate. The calculated aggregate daily systemic exposure to the chemical from oral, dermal and inhalation exposure for face cream including face pump spray was 0.0999 mg/kg bw/day. Based the calculations by SCCS the contribution of inhalation exposure to the systemic exposure dose was minor (0.0001 mg/kg bw/day).

Health hazard information

Toxicokinetics

Based on the molecular weight (<500 g/mol) and partition coefficient, log K_{ow} the chemical is expected to be readily available following oral exposure, and to a lesser extent following dermal exposure. The level of dermal absorption depends on the vehicle and the concentration of the chemical. While the chemical is readily absorbed into the stratum corneum after dermal application; the penetration through the human epidermis is low (Kim et al. 2014; SCCS 2020). Based on calculated vapour pressure inhalation exposure is not expected unless aerosols are formed.

Oral and dermal absorption of homosalate was demonstrated in humans in a study designed to quantify homosalate metabolites in urine. Clear diastereoselectivity in the toxicokinetics of *cis*- and *trans*-homosalate was observed, with the oral bioavailability of the *trans*-homosalate oxidative metabolites exceeding that of the *cis*-homosalate oxidative metabolites by a factor of 10 and the dermal bioavailability of *cis*-isomer was a factor of 2 lower than the *trans*-isomer (Ebert et al. 2022; Ebert et al. 2024).

In a skin penetration study, with a standard sunscreen formulation containing 10% of homosalate conducted according to OECD TG 428, approx. 3.4 mg dose formulation/0.64 cm^2 (corresponding to approx. 0.5 mg homosalate/cm^2) was applied to human skin (12 samples from 4 donors) for 24 hours. Dermal absorption was found to be 3.86 ± 1.43% (5.3% including 1 SD). The dermal absorption from this study was used by the SCCS in their exposure calculations (SCCS 2020).

In another OECD TG 428 (human skin) absorption study using a formulation containing 1% homosalate, absorption was lower (~1%). Based on animal studies, dermal absorption in animals is considered to be higher than human. The mean total absorption was 8.7 ± 2.0% in rats after application of a 10% homosalate containing standard sunscreen formulation (REACH n.d.-a). In an in vivo dermal absorption study in rats the bioavailability of homosalate was 5.4 ± 1.1 and 4.2 ± 0.6% for low and high doses (10 and 20 mg), respectively (Kim et al. 2014).

In a skin penetration study of commercially available sunscreen lotion (SPF 30) containing 8% (w/v) homosalate, the chemical was applied at a rate of 2 mg/cm^2 to an equal sized area (112 cm^2) on the face or back of the volunteers. Blood samples were taken from all volunteers at pre-application baseline and at a suitable steady-state time after application (7.5 hours), and the urine output over 48 hours after application was collected. Homosalate was not detected in the plasma or urine samples of the volunteers in this study (SCCS 2020). However, metabolites were not analysed.

The chemical was detected in human milk after topical application, with maximum plasma concentrations between 13.9 and 23.1 ng/mL and a half-life between 46.9 and 78.4 hours. The chemical was found in three different cohorts (2004, 2005, 2006), in 5.56% of total milk samples. The chemical was used by 15.1% of mothers exclusively in sunscreen with no additional exposure through cosmetic products (SCCS 2020).

Following absorption, homosalate is expected to undergo phase I and phase II metabolism. The primary route of metabolism is likely to be hydrolysis of its ester bond, resulting in the formation of salicylic acid and 3,3,5-trimethylcyclohexanol. The in vitro metabolism of homosalate was investigated in rat and human liver microsomes. Homosalate was primarily hydrolysed into salicylic acid and 3,3,5-trimethylcyclohexanol, other metabolites such as

conjugation and hydroxylation products of intact homosalate was also observed (SCCS 2020). These metabolites were identified using the skin metabolism simulator in the Organisation for Economic Co-operation and Development (OECD) QSAR Application Toolbox (OECD QSAR Toolbox). Salicylic acid is further metabolised through conjugation with glycine to form salicyluric acid, as well as glucuronidation to form salicylic acid glucuronides (AICIS 2024b).

In metabolism studies in humans following oral and dermal exposure the chemical has also been identified unmetabolised and as oxidised metabolites. In studies in human volunteers, *trans*-homosalate was preferentially oxidised into carboxylic acid and alkyl hydroxylated compounds compared to *cis*-homosalate (Ebert et al. 2022; Ebert et al. 2024). While there are differences in the oxidisation of the *cis*- and *trans*- isomers, other metabolites including salicylic acid and 3,3,5-trimethylcyclohexanol were not analysed in these studies, which are thought to be the predominant metabolic products (SCCS 2007).

Salicylic acid is predominantly excreted in urine unchanged or as salicyluric acid. 3,3-5-Trimethylcyclohexanol is primarily excreted as glucuronic acid conjugates. Glucuronides and degradation products are mostly eliminated via urine with minimal amounts eliminated via the faeces (SCCS 2023b).

Acute toxicity

Oral

Based on the available data, the chemical has low acute oral toxicity.

In an acute oral toxicity study conducted according to a procedure recommended by the Association of the Food and Drug Officials of the US, FDRL rats (3 males and 2 females/per dose) were treated with a single dose of the chemical at 0.5, 1.0, 2.0, 4.0 or 8.0 mL/kg bw followed by observations for 14 days. All animals survived the study. Reported sublethal signs of toxicity included diarrhoea, urinary incontinence and emaciation. The median lethal dose LD50 was >8 mL/kg bw (equivalent to 8400 mg/kg bw based on a density of 1.05 g/mL) (SCCS 2007).

In a non-GLP compliant acute oral toxicity study, rats (10 animals, sex unknown) were treated with a single dose of the chemical at 5000 mg/kg bw. The LD50 was >5000 mg/kg bw (REACH n.d.-a; SCCS 2007). No further details are available.

Dermal

Based on the available data, the chemical has low acute dermal toxicity.

In an acute dermal toxicity study, rabbits (10 animals, sex unknown) were treated with a single dose of the chemical at 5000 mg/kg bw. All animals survived the study. The dermal LD50 was determined to be >5000 mg/kg bw (REACH n.d.-a; SCCS 2007).

Inhalation

No data are available.

Corrosion/Irritation

Skin irritation

Based on the available data, the chemical is not expected to be irritating to the skin.

In a GLP compliant in vitro skin irritation study conducted in accordance with OECD TG 439 (in vitro reconstructed human epidermis (RhE) test method for skin irritation), the chemical was applied to RhE for an exposure period of 15 minutes, followed by an observation period of 42 hours. A mean tissue viability value of 108.9% was reported for the chemical in this study. Based on the prediction model criteria the chemical is considered to be a non-irritant to the skin (REACH n.d.-a.; SCCS 2020).

Eye irritation

Based on the available data, the chemical is not expected to be irritating to the eye.

In a GLP compliant in vitro eye corrosion study conducted according to OECD TG 492, the chemical was topically applied to reconstructed human cornea-like epithelium (RhCE) using the EpiOcular^{TM} EIT test method for the liquids and tissue viability was measured following exposure and a post-treatment incubation period. The mean tissue viability was determined to be 94.54%. Based on the decision criteria for this test (tissue viability >60% for EpiOcular^{TM} EIT liquid's protocol), the chemical is considered to not require classification and labelling according to UN GHS (REACH n.d.-a.).

In a GLP compliant eye irritation study similar to OECD TG 405, the chemical (in sunscreen at a concentration of 12%) was instilled into 1 eye each of 3 male New Zealand White (NZW) rabbits. The eyes were washed out after 24 hours and observed at 1, 24, 48 and 72 hours. The following mean scores were reported based on observations at 24, 48 and 72 hours: corneal opacity 0/4, iritis 0/2, conjunctival redness 0/3, chemosis 0/4. No effects were observed on the cornea for any of the rabbits, iritis was reported in 2/3 rabbits after 1 hour of exposure, which was reversible within 24 hours. Conjunctivitis was observed in all rabbits after 1 hour of exposure with slight irritation recorded and the effect was reversible after 72 hours (REACH n.d.-a.; SCCS 2007).

Sensitisation

Skin sensitisation

No guideline studies are available. Based on the available data from non-guideline animal and human studies, the chemical is not expected to be a potent skin sensitiser.

In a non-GLP compliant combined contact and photoallergy study (similar to a Buehler test, OECD TG 406), Dunkin Hartley guinea pigs (10/sex) were induced with the chemical at 1% (w/v) in methanol. After occlusion for 2 hours the patch sites were exposed to UV-A radiation (10 J/cm^2). The animals were challenged with the chemical at 1% (w/v) in acetone with and without irradiation. No skin reactions were observed in any of the animals challenged. The chemical did not cause photoallergy or contact allergy under the conditions tested (REACH n.d.-a; SCCS 2007).

In a non-GLP compliant mouse ear-swelling photoallergy test, epicutaneous induction was performed on 8 female BALB/c mice using the chemical at 10% in acetone or acetone/corn oil (4:1) (not specified). The animals were challenged with the chemical at 5% in acetone or

acetone/corn oil (4:1) (not specified) with and without irradiation at UV-A (10 J/cm^2) and UV-B (30 J/cm^2). The chemical was shown to have no photoallergic, contact allergic or phototoxic potential (REACH n.d.-a; SCCS 2007).

Observation in humans

There was no evidence of skin sensitisation in 10 human repeated insult patch tests. Each study contained more than 100 subjects, were following the same or a comparable test procedure with occlusive and semi-occlusive application and were using different types of sunscreens or other cosmetic products containing homosalate up to 15%. This included one large GLP compliant human repeated insult patch test in 209 volunteers using sunscreen containing 10 or 15% homosalate. Occasional transient erythema was observed during the induction phase. One subject in the 10% homosalate group had a low level reaction at the 48 hour but not at 24, 72 or 96 hour observation. No other skin reactions were observed (SCCS 2007).

Furthermore, no skin reactions were observed in a cumulative skin irritation test in 26 subjects. In these test subjects, homosalate (10 or 15%) was applied to the same site of the back 3 times/week for 6 applications over a 14 day period. Only a few transient minimal skin reactions were observed (SCCS 2007).

In silico

The chemical is predicted to be non-sensitising in OASIS TIMES (Optimised Approach based on Structural Indices Set–Tissue Metabolism Simulator; version 2.3) (OASIS LMC).

The knowledge based expert system Deductive Estimation of Risk from Existing Knowledge (DEREK) Nexus version 6.0.1 (Lhasa Limited) was utilised to estimate the skin sensitisation potential of the chemical. The chemical is predicted positive with an alert for skin sensitisation by substituted phenol reported. Therefore, they are likely to interact with skin proteins by such a mechanism. The predicted effective concentration for a 3-fold increase in lymphocyte proliferation in local lymph node assay (LLNA EC3) for the chemical is 1.2%, indicating moderate skin sensitisation potential.

Repeat dose toxicity

Based on the limited available data, the chemical may have adverse effects on the kidney; however, the effects are not severe enough to warrant hazard classification.

In a combined repeated dose toxicity with reproduction and developmental toxicity screening toxicity study similar to OECD TG 422 (a deviation of constant lighting throughout the study), Wistar rats (10/sex/dose) were administered the chemical via gavage at 0, 60, 120, 300 or 750 mg/kg bw/day for 47 days (males) and 49 days (females).

Mortality only occurred at the highest dose (1 female). Another female was euthanised due to marked bodyweight loss (17%). Clinical signs of toxicity in these females included decreased activity, ruffled fur, uncoordinated movements and hunched posture. Other clinical sign of toxicity was salivation in the two highest dose groups. Food consumption, absolute bodyweights and bodyweight gain were reduced in both sexes at the highest dose.

Statistically significant increases in absolute and kidney to brain weight ratio were reported in females at doses ≥300 mg/kg bw/day. Kidney weights (absolute and relative) were also increased in males at all doses (not dose-dependent). The magnitude of kidney weight

increase was not reported. These changes occurred predominantly at the two highest doses in both sexes. Histopathological findings in the kidney included minimal to moderate increases in intra-epithelial hyaline droplets detected by hematoxylin and eosin (H&E) staining in all males. These changes were associated with an increase in foci of basophilic (regenerating) tubules, single cell death or the presence of granular casts (microscopic bleeding) in a few male rats. Analysis of alpha-2-microglobulin levels was not mentioned in the initial analysis of the study data.

The histological kidney effects were re-evaluated by SCCS in 2020. The SCCS confirmed the presence of hyaline droplets in male rats using a more specific method (immunohistochemistry). The results of their analysis were that the increases in hyaline droplets were minor and mainly present at 120 to 750 mg/kg bw/day. The SCCS analysis was not able to confirm the presence of the kidney lesions described in the initial analysis apart from a single case of necrosis in one cell with hyaline droplets. They observed an increase in alpha-2-microglobulin levels; however, it was only statistically significant in the 120 mg/kg bw/day dose group. They also observed an increase in alpha-2-microglobulin (at comparable levels as males at the same dose) in females exposed to the highest dose of the chemical. Other histopathological findings included single cases of pelvic dilation, pelvic inflammation, mononuclear cell infiltration and tubular basophilia. There was no change in mean cortex area at any dose. Urinalysis tests were not conducted.

Other organ effects included an increase in absolute and relative liver weights at doses above 300 mg/kg bw/day. Thymus weight was decreased in both sexes at the highest dose. Histopathological findings in the liver included minimal or mild centrilobular hypertrophy of hepatocytes in one animal from 120 mg/kg bw/day (1/5 males at 120 mg/kg bw/day, in all males and 4/5 females at 300 mg/kg bw/day, and in all males and 6/7 females at 750 mg/kg bw/day). The thyroid had a higher incidence of diffuse hypertrophy of the follicular epithelium in males dosed at 750 mg/kg bw/day and in females from 300 mg/kg bw/day. Additionally, the thymus had a greater incidence and severity of decreased cortical lymphocytes from 300 mg/kg bw/day and females at 750 mg/kg bw/day.

α2u-Globulin-induced nephropathy (α2u-N) can occur in male rats following exposure to chemicals. Studies across species demonstrate that this response is unique to male rats and not relevant to humans. This response is not typically observed in female rats as typically higher oestrogen levels decrease expression of α2u. In some studies kidney weight changes may be observed in both sexes and it is important to differentiate weight change from droplet accumulation in males to allow identification of the mechanism involved. Based on the re-analysis of the histology of the kidney, SCCS concluded that there was insufficient evidence to determine whether the observed kidney toxicity was dependent on an alpha-2-microglobulin mediated mechanism. This conclusion was based on similar levels of alpha-2-microglobulin in both sexes at the highest dose and that the differences in alpha-2-microglobulin were not statistically significant in males between test item-treated groups and controls. Therefore, the LOAEL of the study was considered to be 60 mg/kg bw/day. The SCCS considered that the presence of constant lighting throughout the duration of the study significantly affected the reliability of the study (SCCS 2020).

In a 15 day repeat dose toxicity study, rats (5/sex/dose; strain not specified) were orally administered the chemical once daily by gavage at 0, 100, 300 or 1000 mg/kg bw/day. In animals that received 100 or 300 mg/kg bw/day of the chemical, there was no relevant effect on body weight, food consumption or food efficiency. A slight gain in body weight and a decrease in food efficiency was observed in male rats administered 1000 mg/kg bw/day. At doses above 300 mg/kg bw/day, reduced coagulation was observed in males. The NOAEL was considered to be 100 mg/kg bw/day (SCCS 2020).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the available data, the chemical is not considered to be genotoxic.

The available data for the chemical indicates that it does not induce gene mutations in bacteria or mammalian cells and does not induce chromosomal aberrations in vitro. No in vivo studies have been conducted with homosalate. The systemic metabolite salicylic acid was negative in vivo studies (REACH n.d.-a).

In vitro

Negative results were reported in the following in vitro genotoxicity studies:

- Multiple reverse mutation assays (OECD TG 471) in *Salmonella(S.) typhimurium* strain TA 98, TA 100, TA 102, TA 1535 and TA 1537 with and without metabolic activation at concentrations up to 10000 µg/plate (SCCS 2007).
- A chromosome aberration test (OECD TG 473) in Chinese hamster V79 cells with and without metabolic activation at concentrations up to 50 µg/mL (SCCS 2007).
- A mammalian cell gene mutation assay (OECD TG 476) in hypoxanthine-guanine phophoribosyl transferase (HPRT) gene in Chinese hamster V79 cells with metabolic activation at concentrations up to 640 µg/mL (SCCS 2007).

Positive results were reported in the following in vitro genotoxicity studies in:

- A non-guideline single cell gel electrophoresis (SGE-comet) assay in human peripheral lymphocytes at concentrations up to 200 µg/mL (SCCS 2020).
- Anon-guideline micronucleus test in MCF-7 human breast cancer cells at concentrations up to 2000 µM (SCCS 2020).

Negative results were reported in the following in vitro photomutagenicity studies:

- A photomutagenicity reverse mutation assay (OECD TG 473) in *S. typhimurium* strain TA 98, TA 100, TA 102 and TA 1537 with continuous irradiation at 0.1– 0.3 mW/cm^2 at concentrations up to 5000 µg/plate. The chemical did not induce gene mutations by base pair changes or frame shifts (REACH n.d.-a; SCCS 2020).
- A photomutagenicity chromosome aberration test (OECD TG 473) in Chinese hamster V79 cells both in the presence and absence of artificial irradiation up to 200 mK/cm^2 at concentrations up to 2.5 µg/mL. The chemical showed no clastogenic potential in the absence of presence of irradiation activation when tested up to cytotoxic concentrations (REACH n.d.-a; SCCS 2020).

In vivo

No data are available for the chemical. Negative results were reported in the following in vivo genotoxicity studies conducted on the likely metabolite salicylic acid:

- A mammalian somatic cell chromosome aberration study similar to OECD TG 475 at concentrations of 350 mg/kg bw. There was no significant increase in chromosome aberrations. However, a significant increase in the mitotic indices was observed (REACH n.d.-a).
- A mammalian sister chromatid exchange assay conducted according to EPA OPPTS 870.5915 at concentrations up to 200 mg/kg bw. No significant increase in sister chromatid exchange was observed (REACH n.d.-a).

In silico

Negative in silico results were reported:

- The knowledge-based expert system DEREK Nexus version 6.0.1 (Lhasa Limited) was utilised to estimate the genotoxicity potential of the chemical. The chemical and its metabolites did not match any structural alerts or examples for (bacterial in vitro) mutagenicity. Additionally, the chemical structure did not contain any unclassified or misclassified features and was; therefore, predicted negative for genotoxicity.
- The chemicals and their metabolites were predicted to be non-genotoxic in in vitro Ames mutagenicity and chromosomal aberrations in OASIS–TIMES (tissue metabolism simulator; version 2.31.2.82) (OASIS LMC). All predictions were in domain of the model.

Carcinogenicity

No data are available for this chemical. The metabolite salicylic acid (NICNAS 2013) and related compound methyl salicylate (AICIS 2024a) are not expected to be carcinogenic. Chronic studies of wintergreen oil (of which methyl salicylate is a major component) also shows no evidence of carcinogenicity (SCCS 2021b).

Reproductive and development toxicity

Limited data are available. In the available study possible effects on fertility and development (reduced fertility index, sperm changes, reduced corpora lutea and higher post-implantation loss) were observed. However, rats in this study were exposed to constant lighting instead of a typical light-dark cycle. Therefore this study cannot be considered as conclusive and reliable. Alterations to the light/dark cycle can adversely affect physiology in many ways including effects on fertility (Emmer et al. 2018; Hoffman 1970). Due to the low number of pregnancies in this study it is not possible to determine whether the chemical affects development. The likely metabolite of homosalate, salicylic acid, caused adverse effects on the animal's development. However, in the absence of further information, it is unclear to what degree the salicylic acid metabolite may contribute to developmental toxicity from homosalate.

In a GLP compliant combined repeated dose toxicity study with reproduction and developmental toxicity screening test similar to OECD TG 422 (a deviation of constant lighting throughout the study), Wistar rats (10/sex/dose) were administered the chemical via gavage once daily at 60, 120, 300 and 750 mg/kg bw/day for a total of 47 days (males) or from 14 days before mating to day 4 of lactation (females), during the premating, mating, gestation and lactation periods.

The fertility index was decreased at all doses, but it was not dose dependent. The following number of pregnancies were recorded: 8/10 in controls, 4/10 at 60 mg/kg bw/day, 5/10 at 120 mg/kg bw/day, 7/10 at 300 mg/kg bw/day and 3/10 at 750 mg/kg bw/day. The number of corpora lutea in individual pregnant females in the highest dose group was lower than in controls and only 1 pup was born live from dams in this group. At 300 mg/kg bw/day, there was a higher incidence of post-implantation loss resulting in a lower birth index; however, litter size was not reduced. Sperm count was not affected at any dose level. However, at the 750 mg/kg bw/day dose, there was a reduction in the number of normal complete sperm (89.5% compared to 97.3% in controls) and sperm motility. There were no effects on sperm morphology or motility at ≤300 mg/kg bw/day.

Post-natal loss was observed at all doses and in the control group. Due to the low number of pregnancies and pups born it is difficult to determine whether the post-natal loss is treatment related. No treatment related findings were noted in pups during the first litter check and during lactation at any dose level. The sex ratio of pups was not affected by the exposure to the test item at any dose level. No macroscopic findings were noted in pups during macroscopical examination at any dose level.

The NOAEL for parental toxicity was 300 mg/kg bw based on effects on food consumption, body weights and mortality at the highest dose. The low numbers of pregnant females, combined with a technical error of constant lighting made it difficult to determine conclusive NOAEL values for the study (SCCS 2020).

The likely metabolite of homosalate, salicylic acid, caused adverse effects on development in rats and monkey including neural tube defects (craniorachischisis), growth retardation and skeletal malformation. The NOAEL for developmental effects based on a study in rats is 75 mg/kg bw/day. The adverse effects on development caused by salicylate are also observed in other salicylates that metabolise to salicylic acid (methyl salicylate and acetyl salicylic acid (AICIS 2024a; AICIS 2024b).

Endocrine effects

The current available data does not provide sufficient evidence of an adverse effect of the chemical from an endocrine mode of action. The chemical was shown to interact with the oestrogen, androgen and progesterone receptors in some in vitro assays, although at potencies several magnitudes lower than endogenously produced hormones. The current available data does not provide sufficient evidence of an adverse effect of the metabolite, salicylic acid, from an endocrine mode of action (AICIS 2024b).

In vitro

An in vitro yeast bioassay reported no or very low oestrogenic activity for salicylate esters used as UV filters and fragrances. The study found that the main criterion for oestrogenic activity is the presence of an unhindered phenolic (OH) group in a *para* position, whereas homosalate, and other salicylic acid esters have a hindered OH group in the *ortho* position (Miller et al. 2001). Based on this result, little eostrogenic activity is expected for homosalate.

In another in vitro assay, homosalate showed the lowest poliferation activity in MCF-7 human breast cancer cells at EC50 of 1.56 µM or 409 µg/L, when compared to various UV filters (Schlumpf et al. 2001).

Schreurs et al (2005) tested for (anti-) eostrogenic activity using 293 HEK cells in vitro and found homosalate to be antagonistic towards the androgen receptor and the progesterone

receptor. According to Krause homosalate seemed not to have been examined for its possible effects on the thyroid axis (Krause 2012).

Kunz and Fent (2006) found that homosalate did not exhibit eostrogenic activity in the human eostrogen receptor alpha (hERα) assay. However, homosalate, among other UV filters, was anti-eostrogenic and completely inhibited the activity of 17 β-estradiol (E2) at the highest concentrations tested, producing a full dose-response curve with a 50% inhibitory concentration (IC50) of 0.00206 M or 540 mg/L. Homosalate also produced a full dose response curve for androgenic activity in the human androgen receptor (hAR) assay (EC50 = 0.00017 M or 44.6 mg/L) as well as anti-androgenic activity via complete inhibition of 4,5-dihydrotestosterone (DHT) activity (IC50 = 0.000107 M or 28 mg/L).

In vivo

No endocrine activity was observed in 2 uterotrophic assays in vivo or in a zebra fish assay (SCCS 2020). In a non-guideline dermal study, juvenile rats were exposed to the chemical during the prenatal, lactation, and early infancy periods. While some hormone fluctuations were reported, these did not correlate with changes in organ function or histology (Erol et al. 2017). Oral administration of homosalate up to the limit dose of 1000 mg/kg bw/day in castrated male rats (Hershberger assay) did not show androgen agonist/antagonist activity or 5α-reductase inhibition (FDA n.d.-b).

Human health risk characterisation

Critical health effects

The critical health effects for risk characterisation are systemic effects (kidney effects).

No NOAEL was determined for the above OECD TG 422 study as kidney effects occurred at the lowest dose (see **Repeat Dose Toxicity – Oral**). The SCCS previously estimated the NOAEL for this study to be 10 mg/kg bw/day. This estimation was derived by applying an assessment factor of 3 to account for LOAEL to NOAEL extrapolation, and then a further 50% reduction due to the lack of information on oral bioavailability (SCCS 2020).

In the absence of other information, the NOAEL of 10 mg/kg bw/day was used for risk characterisation. This NOAEL is considered to be protective of any potential developmental effects.

Public risk

A margin of exposure or MoE methodology was used to characterise the risk to human health associated with systemic exposure to the chemical. The MoE methodology is commonly used to characterise risks to human health associated with exposure to chemicals (ECB 2003).

The MoE risk estimate provides a measure of the likelihood that a particular adverse health effect will occur under the conditions of exposure. As the MoE increases, the risk of potential adverse effects decreases. To decide whether the MoE is of sufficient magnitude, expert judgment is required. Such judgments are usually made on a case by case basis and should consider uncertainties arising in the risk assessment process such as the completeness and quality of available data, the nature and severity of effect(s) and intra/inter species variability.

In general, a MoS value greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences.

There is potentially widespread public exposure to homosalate as it is present in various types of personal care products. The starting points for risk characterisation are external exposure levels estimated based on reported maximum identified international use concentrations (see **Human exposure**).

Table 2 – Margin of exposure (MoE) values for homosalate in cosmetic products at a concentration of 10%.

10%	NOAEL (mg/kg bw/day)	Daily systemic exposure (mg/kg bw/day)	MoE
Face cream	10	0.136	74
Fine fragrances	10	0.066	152
Handcream	10	0.191	52
Lipstick, lip balm	10	0.095	105
Liquid foundation	10	0.045	222
Aggregate exposure (all products)		0.533	19

Based on international use information, homosalate is most frequently used in face cream and lip products (see **Introduction and use**). Based on the worst case scenario estimates when homosalate is used in these products at 10% concentration, the aggregate exposures for face cream and lip products give an MoE of 43 (see **Table 3**). This indicates that homosalate may pose a risk to the public when used at 10% concentration.

Further estimates of systemic exposure to homosalate were conducted to determine the concentration at which the aggregated MoE would be at least 100 (see **Human exposure**). Assuming a maximum concentration of homosalate of 4.35% in both face cream and lip products gave an aggregate MoE of 100 (see **Table 3**).

SCCS concluded that it was safe to use homosalate in face products only at a concentration of 7.34%.

Table 3 – Margin of safety (MoE) values for homosalate from most likely exposure

Product type	MoE at maximum identified concentration (10%)	MoE at reduced concentration (4.35%)
Face cream	74	169
Lip products	105	244
Cumulative (both products)	**43**	**100**

Environmental exposure

High volumes of homosalate are used internationally for a variety of industrial and therapeutic uses. An Australian voluntary call for information from industry identified approximately 159 tonnes of homosalate is being introduced annually to Australia, for use in personal care and sunscreen products. The call for information also identified that homosalate is commonly used in both cosmetics, which are regulated under the *Industrial Chemicals Act (2019),* and therapeutic sunscreens, which are regulated under the *Therapeutic Goods Act (1989)*, with the highest concentrations of homosalate being present in therapeutic sunscreens.

Homosalate functions as a UV filter, fragrance, and skin conditioner in therapeutic sunscreens and a variety of other personal care products. The environmental risks from the use of homosalate in primary and secondary sunscreen products regulated as therapeutic goods are outside the scope of this evaluation. However, their environmental exposure pathways are similar to industrial uses, so it is difficult to distinguish between environmental exposure from therapeutic and industrial uses of homosalate.

Chemicals used in personal care products are typically released to wastewater (e.g. through shower wash off) as a normal part of their use in consumer and commercial applications. Some fraction of the quantity of chemicals in wastewater entering sewage treatment plants (STPs) can be emitted to:

- the air compartment
- rivers or oceans in treated effluent
- soil by application of biosolids to agricultural land (Struijs 1996).

Down the drain release of homosalate is expected to be the main environmental exposure pathway related to its use as an industrial chemical. Homosalate may also be released directly to recreational waters, washing off the bodies of recreational water users while in use. However, this exposure route is expected to be particularly relevant to therapeutic sunscreens. One study indicated that less than 1.4% of applied homosalate is detected in seawater samples from rinse-off during use (Saxe et al. 2021).

Environmental fate

Dissolution, speciation and partitioning

Homosalate is expected to mostly partition to water when released into the environment, with some partitioning to sediment.

Homosalate is only very slightly soluble, and based on its calculated pKa of 9.72, some speciation to the anion is expected in alkaline waters (16% at pH 9). The Henry's law constant indicates only moderate volatility from water and moist soil. Homosalate has high lipophilicity, which promotes partitioning from water to organic matter, including biota and sediment. The calculated K_{OC} of 6,778 L/kg indicates that homosalate will be immobile once it partitions to soil and sediment.

Degradation

Homosalate is inherently and ultimately biodegradable in water and undergoes rapid degradation by hydrolysis. Based on experimental data, homosalate is not persistent.

The key ready biodegradation study in the REACH registration dossier used non-adapted activated sludge according to OECD TG 301F, with the test duration prolonged to 60 days. The degradation was tracked by measuring the oxygen consumption and metabolites were analysed at days 14, 28 and 60 of the study. The mean degradation after 60 days was 62% and thus, the test substance is inherently biodegradable. Specific analysis of the parent compound and metabolites showed fast primary degradation with cleavage of the ester bond resulting in salicylic acid (CAS No. 69-72-7) and 3,3,5-trimethylcyclohexanol (CAS No. 116-02-9) after a short lag phase. Only traces of test item remained after 14 days (REACH n.d.-a). An evaluation of salicylic acid found that it is not persistent and not present in levels that pose a significant risk to the environment (AICIS 2024b). The first degradation step was followed by a lag phase before the second degradation step. The complete mineralisation of the test substance after the second degradation step was confirmed by analytical monitoring of 3,3,5-trimethylcyclohexanone. No residual amounts of 3,3,5-trimethylcyclohexanone were detected in the samples at the end of the 60-day study. This demonstrates that homosalate, and its metabolites, are not persistent (REACH n.d.-a).

In a second experiment the inherent biodegradability was investigated in a test based on OECD TG 302C. No test item specific analysis was performed, and the test was terminated after 28 days, before the biodegradation of the test item reached a plateau. However, the substance exhibited a biodegradation of 70.2% within the 28 day test period. Therefore, homosalate is inherently and ultimately biodegradable (REACH n.d.-a).

The assessment of hydrolytic stability of homosalate was carried out using a procedure designed to be compatible with OECD TG 111 (REACH n.d.-a). The results follow:

- pH 4 Estimated half-life at 25 °C is 210 hours (8.75 days)
- pH 7 Estimated half-life at 25 °C is 215 hours (8.96 days)
- pH 9 Estimated half-life at 25 °C is 69.7 hours (2.90 days).

Homosalate satisfies the criteria for rapid degradation according to the Classification, Labelling, and Packaging (CLP) and the Globally Harmonised System (GHS) (REACH n.d.-a; UNECE 2017) based on a maximum recorded half life of <16 days (~9 days for pH 7). he hydrolysis products, salicylic acid and 3,3,5-trimethylcyclohexanol, also meets the criteria for rapid degradability and are not classified as being hazardous to the aquatic environment.

Bioaccumulation

Homosalate does not meet domestic thresholds for bioaccumulation. Homosalate has a log K_{OW} of 6.27 indicating a potential to bioaccumulate and/or undergo trophic magnification in some aquatic food webs. However, both measured and calculated data indicate that biotransformation occurs at a faster rate than uptake. Bioconcentration factors (BCFs) and

bioaccumulation factors (BAFs) of homosalate, and similar chemicals, are below the domestic threshold for categorisation as bioaccumulative.

Field bioaccumulation studies

Tang et al. (2019) measured homosalate BAFs in wild fish from Lake Chaohu, China. The mean value observed across 6 species of fish was 13.8 L/kg ww, with a range of 4.5–24.0 L/kg ww. He et al (2021) studied homosalate bioaccumulation in red swamp crayfish (*Procambarus clarkii*) and found BAFs of 991 ± 569 L/Kg for homosalate. These values are below the domestic threshold of 2,000 L/kg.

Laboratory and calculated bioconcentration studies

In the REACH registration dossier, homosalate is reported to have a half life of less than one day in fish (REACH n.d.-a). Therefore, a model considering bioelimination from the organism is most suitable and the method of Arnot and Gobas (Arnot and Gobas 2006) was used in EPISuite to take this into account (US EPA 2017a). The calculated BCF estimate in fish (upper trophic level) is 224 L/kg ww (REACH n.d.-a). The lower trophic level BCF for fish is 342 L/kg ww (US EPA 2017b). Calculated BCF values for homosalate are supported by measured and calculated BCF values for analogue chemicals. Cyclohexyl salicylate (log K_{OW} = 4.7, CAS No. 25485-88-5) had a measured BCF between 600 and 900 L/kg ww in *Danio rerio* in steady state, flow-through conditions according to OECD TG 305E (REACH n.d.-b). Ethyl hexyl salicylate (CAS No. 118-60-5) has a measured log K_{OW} of 5.94 (REACH n.d.-c), and the estimated BCF value for ethyl hexyl salicylate based on EPISuite is in the range of 115.6–174.4 L/kg when biotransformation is considered (REACH n.d.-c).

Field biomagnification studies

Yang et al. (2020) calculated trophic magnification factors (TMFs) for pharmaceuticals and personal care products, including UV filters in the highly urbanised Nanjing Qinhuai River system in China. They found a TMF of 1.41 for homosalate, indicating trophic magnification potential in the aquatic food web (Yang et al. 2020). However, TMF studies can be impacted by a range of uncertainties. This study did not use lipid-normalised concentrations in biota, and a contaminant is said to biomagnify when lipid-normalised concentrations of accumulated chemical residues in biological organisms increase with increasing trophic level (Fisk et al. 2001). For this reason, greater weight is placed on the earlier evidence of lack of bioaccumulation.

Environmental transport

Homosalate is not expected to undergo long range transport based on its short half life in the environment. Homosalate was not detected in the Arctic, in a study conducted by Tsui et al. (2014a).

Predicted environmental concentration (PEC)

Based on its use, homosalate is expected to be mainly released into the environment via the sewer with some release directly from the bodies of recreational water users. It has been measured in concentrations ranging from ng/L to low µg/L in a variety of waters internationally. In the absence of Australian monitoring data, a maximum concentration of 345 ng/L in Slovenian rivers has been selected as a conservative PEC. A modelled PEC in soil of 4.46 mg/kg dw has been selected, in the absence of measured data. Homosalate has also been measured in a variety of sediment studies, up to a maximum concentration of

26 ng/g dw in the sediment of Japanese streams and rivers. This value will be used as a conservative PEC for risk characterisation purposes in Australia. Given its presence in waters and sediment, levels of homosalate have also been detected in biota, and these have been reported for information purposes in this section.

Soil and surface waters

A major source of environmental exposure of homosalate is via the sewer. Based on a reported introduction volume of 159 tonnes/annum, 100% release to sewers, and modelled sewage treatment, a concentration of 8.57 µg/L is predicted in STP effluent. Modelled partitioning of 78% to biosolids predicts a concentration of 668 mg/kg dw (SimpleTreat 3.0) (Stuijs 1996). This biosolid concentration, under a standard model of application of biosolids to agricultural land, produces a PEC in soil of 4.46 mg/kg dw. Regarding sewage treatment, Tsui et al (2014b) investigated the influent concentrations, effluent concentrations, and removal efficiency of different sewage treatment plants and treatment techniques. Homosalate showed more than 99% removal under reverse osmosis, 76% removal via chlorination, and more than 70% removal under secondary treatment. SimpleTreat modelling assumes 90% removal and may under or overestimate effluent concentrations depending on treatment techniques employed. However, the predicted effluent concentration and soil PEC are expected to be overestimates of the concentrations resulting from industrial uses as the reported Australian volume is for both industrial and therapeutic uses of the chemical.

As well as release via sewers, homosalate is also released directly into the aquatic environment from the bodies of recreational water users. Therefore it has been detected in a range of aquatic environments including beaches, reefs, rivers, lakes, and streams as summarised in the following paragraphs.

Homosalate has been measured in a variety of surface waters internationally. Tashiro and Kameda (2013) measured the concentrations of UV filters at four beaches, two reefs, and one river on Okinawa Island, Japan. Concentrations at beaches ranged from not detected up to 214 ng/L and peaked in the warmest part of summer, likely corresponding to use in sunscreens with high homosalate concentrations. Most measurements for homosalate at the reefs and river were not detected, with a maximum of 3.2 ng/L reported at a reef site. These values were comparable to the maximum concentration of 29 ng/L found in streams, STP effluents, lakes, and moderately and heavily polluted rivers within an urban area in Saitama Prefecture, Japan (Kameda et al. 2011). Cuderman and Heath (2007) measured homosalate in Slovenian river waters at up to 345 ng/L but did not detect it in the studied lakes (LOD 194 ng/L). O'Malley et al. (2021) attempted to measure homosalate in the suite of UV filters studied at an Australian recreational water body. However poor sensitivity and other analytical problems prevented the monitoring c. Without any Australian monitoring data, the predicted environmental concentration in domestic surface waters from diffuse release via STPs is conservatively taken to be 345 ng/L as reported for Slovenian river waters. This value was the highest found internationally that was not attributed to transient and localised releases. As such, it is conservatively representative of the release of homosalate down the drain.

Other international monitoring of homosalate levels in the surface waters of cities, beaches and reefs is available. Tsui et al (2014a) measured the occurrence of UV filters in surface waters in Hong Kong, Tokyo, Bangkok, New York, Los Angeles, the Arctic, Shantou, and Chaozhou. Total UV filter concentrations generally decreased with population density. Homosalate was detected in 76% of the 60 Hong Kong Harbour samples in the range of 66-2812 ng/L. The concentrations of homosalate exceeding 1000 ng/L were in surface water samples collected on hot summer days with strong UV radiation in June and August 2013 at a popular beach in Hong Kong, indicating use and wash-off from sunscreens high in

homosalate content. Given the significant population density in this region, the monitoring values are unlikely to be relevant to Australian conditions. Concentrations of homosalate in the other major cities studied ranged 29–270 ng/L (Tsui et al. 2014a).

For coral reef locations, Barger et al. (2015) measured UV filter concentrations in several bays of the US Virgin Islands. Homosalate was found at a maximum of 1413 ng/L in Trunk Bay, which is subject to heavy tourism. Sanchez Rodriguez et al. (2015) measured homosalate at concentrations ranging 2.4–536 ng/L at Canary Island beaches. Mitchelmore et al. (2019) reported homosalate concentrations up to 625.7 ng/L at reefs off Oahu, Hawaii. Tsui et al. (2019) found homosalate from 3.6-41.84 ng/L at coral reefs in Hong Kong. Another study reported homosalate concentrations of 15.5–187.9 ng/L in the waters of the Chesapeake Bay estuary in the United States (He et al. 2019).

Sediment

Being lipophilic, homosalate partitions to sediment and biota. Therefore, it has been measured in a range of aquatic sediments and biota around the world, as reported below.

Kameda et al. (2011) measured the concentrations of UV filters in the sediment of streams, STP effluents, and moderately and heavily polluted rivers. The authors detected homosalate in the sediment of streams up to 26 ng/g dw, moderately polluted rivers up to 0.8 ng/g dw, and in heavily polluted rivers up to 6 ng/g dw. Apel et al. (2018) detected homosalate in the surface sediment of the Bohai Sea and Yellow Sea between 0.06-0.94 ng/g dw. Pintado-Herrera et al. (2017) found homosalate in sediments of Cadiz Bay and Huelva Estuary in Andalusia, Spain up to 8.5 ng/g dw. He et al. (2019) reported homosalate up to 74.2 ng/g dw in the sediment of Chesapeake Bay. Mitchelmore et al. (2021) conducted a review of UV filters around coral reefs and reported a median of 5.05 ng/g dw of homosalate in sediments near Hawaiian coral reefs (Mitchelmore et al. 2019), while Tsui et al. (2015) did not detect homosalate in reef sediments and Apel et al. (2018) found the median below the limit of quantification. The maximum value of 26 ng/g dw is conservatively selected as the PEC for sediment in Australia.

Biota

Homosalate has also been detected in a range of aquatic biota globally. Mitchelmore et al. (2019) measured a median of 341 ng/g dw in corals around Hawaii, USA. Homosalate was measured in fish in Germany at a maximum concentration of 3100 ng/g dw (lipids) (Nagtegaal et al. 1997). Tang et al (2019) found concentrations of homosalate in the muscle of wild fish from Lake Chaohu, China, ranging 0.13-11.0 ng/g dw. Cunha et al. (2018) studied levels of homosalate in seafood, reporting the highest levels in wild tuna at 58.5 µg/kg dw. Homosalate was reported at up to 158.3 ng/g dw in the tissue of oysters from Chesapeake Bay (He et al. 2019). Homosalate was detected in oysters on the Portuguese coast at up to 45 ng/g dw (Gadelha et al. 2019). This data shows that homosalate makes its way from the environment into biota at low levels.

Environmental effects

Effects on aquatic Life

Acute toxicity

With low solubility and a high log K_{OW}, homosalate is a difficult to test substance. Acute ecotoxicity testing, using homosalate or ethyl hexyl salicylate (EHS, CAS No. 118-60-5) as a

suitable analogue, reported in the REACH registration dossier for fish, invertebrates, and algae found no effects at saturation (REACH n.d.-a). This is supported by acute toxicity testing on *Daphnia*, which found no effects at 50% of water solubility (Layton 2015). One study, employing a solvent to solubilise the homosalate, found a 48 hour LC50 of 2.4 mg/L, which is above the test substrate's solubility limit (Thorel et al. 2020).

Chronic toxicity

The following measured and calculated no observed effect concentration (NOEC) values were retrieved from the REACH registration dossiers for homosalate (algae), and the analogue chemical EHS (invertebrates) (REACH n.d.-a; REACH n.d.-c). A calculated chronic endpoint has been included for fish using EPISuite (US EPA 2017a). EHS is considered a suitable analogue due to the similar salicylate ester structure, similar numbers of carbons, and similar physical and chemical properties (water solubility = 0.074 mg/L, log K_{OW} = 5.94).

Taxon	Endpoint	Method
Fish	NOEC = 0.006 mg/L	ECOSAR ChV Neutral Organics and Phenols Class Calculated for homosalate
Invertebrates	21 d NOEC = 0.006 mg/L	*Daphnia magna* (water flea) Reproduction Nominal concentrations OECD TG 211 Analogue substance EHS
Algae	72 h NOEC > 0.0089 mg/L	*Daphnia magna* (water flea) Reproduction Nominal concentrations OECD TG 201

The chronic calculated endpoint for fish has been included as ECOSAR has been shown to give the most conservative value from multiple models for the analogue EHS (REACH n.d.-a) which has been verified with comparison to experimental values for other salicylate analogues. Layton (2015) tested homosalate for chronic toxicity to *Daphnia magna* finding effects on mean neonates per surviving adult at all tested concentrations. This includes a small but significant hormetic positive effect at the lowest concentration of 0.075 mg/L and a negative effect on fecundity at 0.3 mg/L in a 21 day test. However, these effects were observed from nominal concentrations above the solubility of homosalate, not from measured homosalate concentrations within the water solubility limits. Therefore, they are given less weight than standardised testing of the EHS analogue.

Thorel et al. (2020) conducted a 7 day study and found a LC50 of 0.074 mg/L for algae, with significant effects for a non-apical endpoint at 0.010 mg/L. Although it is noted that this was not a guideline study, not conducted in a GLP laboratory, and a solvent was used, this does give weight to the above chronic toxicity data and the chronic classification for toxicity.

Effects on sediment dwelling life

No ecotoxicity data are currently available for effects on sediment dwelling life. For the purposes of this risk assessment the ecotoxicity to aquatic life has been determined via the equilibrium partitioning method (EPHC 2009), to give an indication of levels in sediment that may produce effects on sediment dwelling and/or aquatic life (see **Predicted no effect concentration (PNEC)** section). Lucas et al. (2022) found homosalate did not induce any significant effect on fish embryos developed from eggs exposed to sediment spiked with

homosalate under their exposure conditions (96 hr and 10 µg/g homosalate) regardless of the physiological endpoint studied.

Some UV filters have been investigated for hazards to corals (see reviews by Mitchelmore et al. 2021 and Moeller et al. 2021). According to Miller et al. (2021), homosalate does not present a risk to coral up to the limit of water solubility. Stien et al. (2020) found that homosalate does not alter either the concentration of a coral growth hormone (compound 14) or the overall metabolome of *Pocillopora damicornis*. However, polyps of coral exposed to homosalate at 1 mg/L were closed at the end of the assay, while those of control corals were not. This was interpreted as the coral reacted to the substance, although its metabolome was not significantly altered. It is neither a negative, nor an apical, endpoint and it is notable that the test concentration was approximately a factor of 10 greater than the solubility limit of homosalate.

Effects on terrestrial life

No terrestrial ecotoxicity data are currently available for homosalate. The ECHA Chem dossier reports cyclohexyl salicylate as an acceptable analogue for read across based on structural similarity, with data available for three trophic levels (ECHA Chem n.d.-b).

A LC50 value between 560 and 1000 mg cyclohexyl salicylate/kg soil dw was reported for *Eisenia fetida* (earthworm) mortality after 14 days exposure, as per OECD TG 207 (REACH n.d.-b). This corresponds to an LC50 of 667–1191 mg homosalate/kg soil dw when converted based on molecular weight. However, the study notes no mortality was recorded at 560 mg cyclohexyl salicylate/kg soil dw and 60% mortality was observed on day 7 for 1000 mg cyclohexyl salicylate/kg soil dw.

A 28 day test on *Avena sativa* (oats) per OECD TG 208 reported a NOEC value of 300 mg cyclohexyl salicylate/kg soil dw and LOEC value of 1000 mg cyclohexyl salicylate/kg soil dw (REACH n.d.-b). The NOEC value correlates to 357 mg/kg soil dw for homosalate.

In a 28 day test on soil microorganisms as per OECD TG 216 no effects were observed up to the final test value of 100 mg/kg soil dw (REACH n.d.-b). The final test value converts to 119 mg/kg soil dw for homosalate.

Endocrine activity

Homosalate is listed on the Endocrine Active Substances Information System (EASIS n.d.). There is evidence that homosalate interacts with endocrine systems but limited evidence of adverse effects, even at high doses.

Kunz and Fent (2006) found that homosalate did not exhibit eostrogenic activity in the human eostrogen receptor alpha (hERα) assay but showed anti-eostrogenic, androgenic activity and anti-androgenic activity (see **Human Health effects: Endocrine activity**). Concentrations at which effects were observed significantly exceed the water solubility limit of homosalate and environmentally relevant concentrations. Overall, homosalate had maximal dose response curves with more than 80% efficacy for anti-eostrogenic, androgenic and anti-androgenic activity. Kunz and Fent (2006) found no effect for *in vivo* vitellogenin induction for homosalate in the rainbow trout eostrogen receptor alpha (rtERα) and hERα assay comparisons for fish. They concluded that the eostrogenic activity of most benzophenones and salicylates seems to be abolished in vivo because of metabolism. The endocrine effects of UV filters have been shown to be additive in multiple studies of mixtures (e.g. Kunz et al. 2006, Kunz and Fent 2009), as a caution to applying individual results to risk assessment. Kunz et al. (2006) used

in vitro recombinant yeast assays, whereas Kunz and Fent (2009) used in vivo assays with fathead minnows.

Salicylate ions are a metabolite and environmental degradant of homosalate. As per the evaluation of salicylic acid (AICIS 2024b), there is evidence that salicylate interacts with endocrine systems but there is limited evidence of adverse effects, even at high doses. There are relatively few studies available on endocrine effects in more environmentally relevant organisms. There is currently no evidence to suggest harmful effects in the environment. While some studies indicate that high concentrations of salicylate may interact with the thyroid hormone system, this is considered to have low environmental relevance.

Predicted no-effect concentration (PNEC)

A freshwater PNEC of 0.6 µg/L (600 ng/L) is derived for homosalate from the measured invertebrates chronic ecotoxicity endpoint (21d NOEC = 0.006 mg/L) for the analogue ethyl hexyl salicylate, using an assessment factor of 10. This assessment factor was selected as reliable measured and calculated chronic ecotoxicity data are available for homosalate, or the ethyl hexyl salicylate analogue, for three trophic levels (EPHC 2009).

A sediment PNEC of 163 µg/kg dw has been derived for homosalate by the equilibrium partitioning method using the aquatic PNEC of 0.6 µg/L, the calculated K_{OC} of 6,778 L/kg, and default values (EPHC, 2009).

A soil PNEC of 7.14 mg/kg dw (7,140 µg/kg dw) is derived for homosalate based on the analogue-derived NOEC of 357 mg/kg dw soil for terrestrial plants and an assessment factor of 50. This assessment factor was chosen as terrestrial ecotoxicity data for the suitable analogue, cyclohexyl salicylate, was available for a short term test and two long term tests for three trophic levels (EPHC, 2009).

Categorisation of environmental hazard

The categorisation of the environmental hazards of the assessed chemical according to domestic environmental hazard thresholds is presented below:

Persistence

Not Persistent (Not P). Based on measured biodegradation and hydrolysis data, homosalate is categorised as Not Persistent.

Bioaccumulation

Not Bioaccumulative (Not B). Based on measured and calculated BCF and BAF values in fish, and evidence of biotransformation, homosalate is categorised as Not Bioaccumulative.

Toxicity

Toxic (T). Based on chronic toxicity values below 0.1 mg/L for a suitable analogue chemical, homosalate is 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 homosalate to surface waters, sediments, and soils:

Compartment	PEC	PNEC	RQ
Surface water (effluent, rivers, etc)	345 ng/L	600 ng/L	0.575
Sediment	26 µg/kg dw	163 µg/kg dw	0.16
Soil	4,460 µg/kg dw	7,140 µg/kg dw	0.62

For surface waters, sediment and soil, an RQ less than 1 indicates that homosalate is not expected to pose a significant risk to the environment based on estimated diffuse emissions and environmental monitoring, as environmental concentrations are below levels likely to cause harmful effects. However, re-evaluation of homosalate may be required if Australian monitoring data with environmental concentrations higher than those considered in this Evaluation Statement or relevant ecotoxicity data for the sediment compartment become available.

Homosalate is categorised as not persistent, not bioaccumulative and toxic. The log K_{OW} of homosalate indicates bioaccumulation potential, but the bioconcentration and bioaccumulation factors (BCF & BAF) of homosalate and similar chemicals are below the domestic threshold for categorisation as bioaccumulative. Homosalate has also been reported to interact with the endocrine system in several studies, but only at concentrations that far exceed concentrations that are likely to occur in the environment.

International monitoring data suggests that some recreational water bodies, such as popular beaches and reefs, may be subject to transient elevated concentrations of homosalate through its use in personal care products and sunscreens. The highest monitoring values were identified for areas that were subject to high population densities and/or heavy recreational use, particularly in summer months. Conservative worst case assumptions for these locations would result in localised RQs >1, indicating the presence of transient risks. However, there are no acute effects expected at the limit of water solubility, the chemical is rapidly degradable and will be dispersed within the water bodies, thus limiting the potential for environmental risks. These concentrations include contributions from the wash-off of therapeutic sunscreens, including those with higher homosalate content, which are not regulated as industrial chemicals in Australia. In the absence of Australian specific monitoring data linking concentrations to different classes of products, there is insufficient evidence to characterise the risk to the environment at these locations from either the industrial or the therapeutic uses of homosalate.

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 discussed below:

- The risk characterisation for homosalate is based on the most relevant international monitoring data that is available. There is no Australian monitoring data for homosalate.
    - Further evaluation may be required if Australian monitoring or exposure data become available to indicate that it may be present in Australian surface waters, sediments, or soils at concentrations above the levels of concern.
- There are no standard ecotoxicity data on sediment dwelling organisms or terrestrial species available for homosalate. Additionally, the ecotoxicity to other potentially sensitive aquatic organisms, such as coral and sea urchins, has been studied but not fully characterised by standardised international methods.
    - The ECHA Chem dossier for homosalate states that the screening assessment indicates the need to investigate further the effects on sediment organisms, and a testing proposal for a Sediment-Water Lumbriculus Toxicity Using Spiked Sediment according to OECD TG 225 is proposed. Depending on the results of the OECD 225 study further sediment toxicity tests might be suggested. The ECHA Chem dossier and the risk assessment will be updated as soon as the results are available (ECHA Chem n.d.-a).
    - Further evaluation may be required if new ecotoxicity data become available indicating that homosalate is more hazardous than considered in this evaluation.
- The endocrine activity and effects of homosalate have been studied but not fully characterised by standardised international methods.
    - Further evaluation may be required if new relevant data become available.
- The identities and environmental effects of the degradation products of homosalate have not been fully assessed as part of this evaluation.

Further evaluation may be required if more information becomes available in the future to indicate the potential for any environmental metabolites or degradants to cause harm in the environment.

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