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

2-Propenoic acid, 2-cyano-3,3-diphenyl-, 2-ethylhexyl ester (Octocrylene)

Evaluation statement (EVA00182)

31 March 2025

Draft

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AICIS evaluation statement (EVA00182)

Subject of the evaluation

2-Propenoic acid, 2-cyano-3,3-diphenyl-, 2-ethylhexyl ester (Octocrylene)

Chemical in this evaluation

CAS name	CAS number
2-Propenoic acid, 2-cyano-3,3-diphenyl-, 2-ethylhexyl ester	6197-30-4

Reason for the evaluation

Evaluation Selection Analysis indicated a potential human health risk.

Parameters of evaluation

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

This evaluation statement includes a human health risk assessment for all identified industrial uses of 2-propenoic acid, 2-cyano-3,3-diphenyl-, 2-ethylhexyl ester (octocrylene). The use of octocrylene in therapeutic sunscreens is not assessed in this evaluation because this is not an industrial use.

Benzophenone is a known manufacturing impurity and degradation product of octocrylene. The risks from exposure to benzophenone through use of octocrylene have been evaluated in our evaluation for benzophenone (EVA00184, AICIS 2025).

Summary of evaluation

Summary of introduction, use and end use

Based on available information, octocrylene is used in a range of personal care products (cosmetics), including skin applied products such as secondary sunscreen products, perfumes and body sprays 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.

Based on the limited available data, the chemical:

- has low acute oral and dermal toxicity
- is not irritating to the eyes or the skin
- is not expected to have genotoxic potential.

Based on the available data, the chemical is a potential skin sensitiser, with low to moderate potency in animal tests. In a local lymph node assay (LLNA) performed conducted similar to OECD TG 429, the reported concentration producing a three fold increase in lymphocyte proliferation (EC3) was found to be 7.7%. However, there is a low incidence of sensitisation cases to octocrylene in humans, despite widespread use. Occurrence of photoallergy to octocrylene is strongly related to a previous photoallergy to topical ketoprofen.

In oral studies available, reduced body weights, increased liver weights, increases in hypertrophic cells in the pituitary glands and thyroid was observed at high doses. The severity of the adverse effects or doses at which effects were observed in various organs is not sufficient to warrant hazard classification.

Based on the available data, the chemical may cause adverse effects on fertility. A reduced number of implantation sites and lower number of pups delivered were observed in an extended one generation reproductive toxicity study (EOGRTS) and range finding study. The effects were observed only in the high dose groups together with mild systemic toxicity in dams. There was no evidence of specific developmental effects in the available studies.

Current available data do not provide sufficient evidence of an adverse effect of the chemical from an endocrine mode of action.

No carcinogenicity data are available for the chemical. There is sufficient evidence that the impurity/breakdown product benzophenone has carcinogenic effects in animals. The available data supports a likely threshold mode of action.

No data are available for acute or repeated dose inhalation toxicity. For further details of the health hazard information see **Supporting Information**.

Hazard classifications relevant for worker health and safety

This chemical satisfies the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant for work health and safety as follows. This evaluation does not consider classification of physical hazards and environmental hazards.

Health hazards	Hazard category	Hazard statement
Skin sensitisation	Skin Sens. 1B	H317: May cause an allergic skin reaction
Reproductive toxicity	Repro Tox. 2	H361f: Suspected of damaging fertility

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

The chemical may cause adverse effects on fertility. A margin of exposure (MOE) methodology was used to characterise the risk to human health associated with systemic exposure to the chemical. Based on the worst case scenario estimates when octocrylene is used in a range of personal care products (cosmetics) at 10% concentration, a MOE of 110 was calculated. In general, an MOE value greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences. This indicates that octocrylene is unlikely to pose a risk to human health if used in cosmetic products at current use concentrations of 10% or less.

There is a low incidence of cases of sensitisation to octocrylene in humans, despite widespread use. Occurrence of photoallergy to octocrylene is strongly related to a previous photoallergy to topical ketoprofen. Topical ketoprofen use in Australia is not expected to be widespread. Therefore the chemical is considered unlikely to pose a significant risk of skin sensitisation and photosensitisation under the current use patterns.

Based on the worst case scenario estimates from products containing octocrylene, the aggregate systemic exposure to benzophenone as an impurity/breakdown product is 0.013 mg/kg bw/day. This estimate is approximately a third of the Tolerable Daily Intake (TDI) recommended by EFSA. EFSA considered this TDI sufficiently protective for the non-neoplastic effects in repeat dose toxicity studies and the neoplastic effects in the carcinogenicity studies

Overall, there are no risks to the public from industrial use of the chemical that require management. The need for risk management for the impurity or breakdown product is being considered as part of another evaluation (AICIS 2025).

Workers

During product formulation and packaging, dermal, ocular and inhalation exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and in the cleaning and maintaining of equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic long term effects, the chemical could pose a risk to workers unless adequate control measures to minimise dermal and inhalation exposure are implemented (see **Proposed means for managing risk**).

Proposed means for managing risk

Workers

Recommendation to Safe Work Australia

It is recommended that Safe Work Australia (SWA) update the Hazardous Chemical Information System (HCIS) to include classifications relevant to work health and safety (see **Summary of Health Hazards Section**).

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:

- using closed systems or isolating operations;
- 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.

These control measures should be supplemented with:

- conducting health monitoring for any worker who is at significant risk of exposure to the chemical, if valid techniques are available to monitor the effect on the worker's health.

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

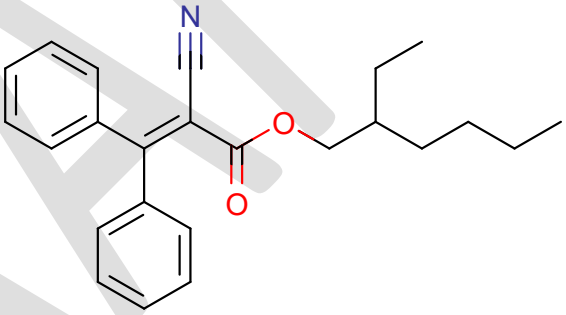
The Executive Director proposes to be satisfied that the identified risks to human health from the introduction and use of the industrial chemical can be managed.

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	6197-30-4
CAS name	2-Propenoic acid, 2-cyano-3,3-diphenyl-, 2-ethylhexyl ester
Molecular formula	$C_{24}H_{27}NO_2$
Associated names	2-Ethylhexyl-2-cyano-3,3-diphenylacrylate Octocrilene Octocrylene
Molecular weight (g/mol)	361.48
SMILES (canonical)	N#CC(C(=O)OCC(CC)CCCC)=C(C=1C=CC=CC1)C=2C=CC=CC2
Structural formula	

Relevant physical and chemical properties

Physical form	Liquid
Melting point	-10 °C
Boiling point	Substance decomposes before boiling
Vapour pressure	0 hPa 25 °C
Water solubility	9 - 153 µg/L
Ionisable in the environment?	No
log K_{ow}	6.1 at 23 °C

Introduction and use

Australia

Octocrylene is a UV filter which absorbs primarily UVB radiation and short UVA wavelengths. It is used in various cosmetic products to either provide sun protection in sunscreen products or to protect cosmetic formulations – such as photosensitive pigments from UV radiation. Octocrylene 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.

Personal care products (cosmetics) containing octocrylene, including face cream, moisturiser, nail polish, suntan products (that are not primary sunscreens) and lip balm, have been identified on Australian commercial websites.

The chemical has reported frequent use in therapeutic sunscreens.

International

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

- face cream
- foundation
- lip balm
- hand cream
- concealer
- massage products
- perfume/ eau de toilette
- tanning products (that are not primary sunscreens)
- makeup primer
- body spray.

Octocrylene is primarily used as an active ingredient in personal care products (cosmetics) where it functions as a light stabiliser or UV-filter. Based on international data the personal care products that are most likely to contain octocrylene are face cream, foundation, nail polish remover and lip balm (Danish EPA 2015; INCI beauty n.d.; De Lima Associates n.d.; EWG n.d.). 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, body spray, foundation and face creams.

Use of whole-body leave-on tanning products (that are not primary sunscreens) and massage products 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, octocrylene was found in 76 out of 291 products. Of these, the majority were likely to be used in therapeutic sunscreens (53). However, octocrylene was also reported to be used in 12 face creams, 4 foundation products, 3 make up, 1 hand cream, 1 lip balm, 1 sun oil and 1 nail polish remover. The chemical is listed on the International Fragrance Association (IFRA) Transparency List (IFRA n.d.).

Existing Australian regulatory controls

Public

The chemical has restrictions for its non-industrial use in therapeutic sunscreens and is 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.

Octocrylene

- 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 10%.

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.).

International regulatory status

Canada

The chemical is listed in the Primary Sunscreen Monograph, non-prescription drug medicinal ingredients at concentration ≤10% currently allowed (Government of Canada 2022).

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. Octocrylene is permitted in propellant spray products at a concentration of 9% and 10% in other products. Benzophenone as an impurity or degradation product should be kept at a trace level of 0.5% (EC n.d.).

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 10% for over the counter sunscreen drug products for human use (FDA n.d.).

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 states in "Appendix 4: The ingredients are restricted in all types of cosmetics" and that total concentration of octocrylene 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

Exposure to octocrylene

As octocrylene 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 use of 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.

The public exposure to octocrylene 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 based on identified use product categories (see **Introduction and use**). For the exposure assessment, the use amounts were determined using values established by the SCCS (SCCS 2023) and RIVM (RIVM 2006). Body lotion values were considered indicative of exposure through use of massage oil and tanning products (that are not primary sunscreens). A default body weight (BW) of 60 kg was used.

For oral exposure from lip products (see **Table 1**), the daily systemic exposure dose was calculated based on daily product amounts, product retention factors (RF) (reflecting proportions of product remaining on the skin during normal use) and oral bioavailabilty (OA). An oral absorption value of 50% was assumed (see **Toxicokinetics**).

Table 1: Daily systemic exposure to octocrylene from lip products

Type of product	Amount (mg/day)	C (%)	RF (unitless)	OA (%)	Daily systemic exposure (mg/kg bw/day)
Lipstick, lip balm	57	10	1	50	0.048

Daily systemic exposure = (Amount × C × RF × OA)/BW with BW = 60 kg
C = chemical concentration; RF = retention factor; DA = dermal absorption; BW = body weight

For dermal exposure (see **Table 2**), the daily systemic exposure dose was calculated based on the skin surface area (SSA), frequency of application (F), concentration (C) and dermal absorption (DA). A dermal absorption value of 0.97 µg/cm^2 was used (see **Toxicokinetics**).

Table 2: Daily systemic exposure to octocrylene from dermally applied cosmetic products based on the currently maximum allowed concentration in EU.

Type of product	Skin Surface Area (SSA) (cm^2)	C (%)	Frequency of application (F) (per day)	DA (µg/cm^2)	Daily systemic exposure (mg/kg bw/day)
Body lotion	15,670	10	2.28	0.97	0.577
Face cream	565	10	2.14	0.97	0.019
Fine fragrance	200	10	1	0.97	0.003
Hand cream	860	10	2	0.97	0.027
Liquid foundation	565	10	1	0.97	0.009
Nail varnish remover	11	10	1	0.97	0.0001
Total					**0.637**

Daily systemic exposure = SSA*C*F*DA*0.001/BW with BW = 60 kg
SSA = skin surface area; C = chemical concentration; F = frequency of application; DA = dermal absorption; BW = body weight

Overall using the worst case exposure scenario from use of multiple products simultaneously by an individual consumer the exposure is estimated to be 0.68 mg/kg bw/day.

Exposure to benzophenone

Benzophenone is a known manufacturing impurity and degradation product of octocrylene. Octocrylene can undergo retro-adol condensation which is catalysed under acidic or basic conditions and can be accelerated in the presence of protic solvents such as water. Commercially available sunscreen products were found to be contaminated with benzophenone, with an average concentration of 39 mg/kg benzophenone, ranging from 6 mg/kg to 186 mg/kg. These products also underwent a 6 week accelerated stability aging protocol according to US FDA regulations and benzophenone was found with an average

concentration of 75 mg/kg, ranging from 9.8 mg/kg to 435 mg/kg, equating to a 14.5% to 199.4% increase from baseline (Downs 2021).

Based on the worst case scenario estimates from products containing octocrylene, the aggregate systemic exposure to benzophenone as an impurity or breakdown product is 0.013 mg/kg bw/day (AICIS 2025).

Health hazard information

Toxicokinetics

Based on the molecular weight (<500 g/mol) and partition coefficient (log K_{ow} = 6.1) 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 but is generally low (SCCS 2021). Based on calculated vapour pressure inhalation exposure is not expected unless aerosols are formed.

In a GLP compliant dermal absorption study, with a standard sunscreen formulation containing 10% of octocrylene conducted according to OECD TG 428, 3 mg/cm^2 was applied to human skin (12 samples from 6 donors) for 24 hours. Dermal absorption was reported to be 0.45±0.52 µg/cm^2 (0.97 µg/cm^2 including 1 SD).

The chemical was detected in human milk after topical application with cosmetic products containing octocrylene, with maximum plasma concentrations at 30.18 ± 24.51 ng/g of lipids (Schlumpf et al. 2010).

Available toxicity data (see **Repeated dose toxicity**) indicate the capacity of octocrylene to induce xenobiotic-metabolising enzymes. Therefore, a significant metabolism of octocrylene in the liver is expected when being absorbed from the gastrointestinal tract.

The following metabolic pathway is expected:

- hydrolysis of the ester linkage by esterases to form 2-cyano-3,3-diphenyl-2-propenoic acid (commonly abbreviated to CDAA) and 2-ethylhexanol
- oxidation of both hydrolysis products by cytochrome P450-dependent monooxygenases
- cytochrome P450-dependent decarboxylation of 2-cyano-3,3-diphenyl-2-propenoic acid
- glucurono-/ Sulfo- or GSH-conjugations of metabolic oxidation products.

Octocrylene and six metabolites were reported to be detected in human urine after both oral and dermal exposure. The major urinary metabolite was identified as CDAA (~45% of the octocrylene dose) (Bury et al. 2019). Octocrylene detection rates in urine was low with 81% of samples below the limit of detection. However, CDAA was readily detected in urine, with the maximum concentration between 71.4–2072 µg/g creatinine, the peak concentration was found after 16–48 hours and a half-life of 38 hours. Overall, approximately 50% of the oral dose was recovered in urine indicating that a significant amount of the chemical is excreted in the faeces.

Following dermal sunscreen exposure, Octocrylene and CDAA were detected in all plasma samples investigated. The maximum plasma levels of octocrylene were found to be between 0.5–11.7 ng/mL, with peak concentrations after 10–74.5 hours and a half-life of between

43.3–84.4 hours. The maximum plasma concentration of CDAA has been reported to be 570 ng/mL with a peak concentration after 15 hours and a half-life of 36 hours (Matta et al. 2020; Hillier et al. 2019).

Acute toxicity

Oral

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

In a GLP compliant acute oral toxicity study conducted according to OECD TG 401, Wistar rats (5/sex/dose) were treated with a single dose of the chemical at 5000 mg/kg bw. No adverse effects were noted. The LD50 was >5000 mg/kg bw (REACH n.d.-a; SCCS 2021).

Dermal

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

In a GLP compliant acute dermal toxicity study conducted according to OECD TG 402, Sprague Dawley rats (5/sex/dose) were treated with a single semi-occluded dermal application of the chemical at 2000 mg/kg bw. After 14 days of observation there were no deaths, signs of systemic toxicity or skin irritation. The LD50 was >2000 mg/kg bw (REACH n.d.-a; SCCS 2021).

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 skin irritation study conducted in accordance with OECD TG 404 New Zealand White (NZW) rabbits (4 animals, sex unknown) were treated with the chemical for 4 hours under semi-occlusive conditions. Observations were recorded at 24, 48 and 72 hours after patch removal. The following mean scores were reported for observations at 24, 48 and 72 hours: (0,0,0) for erythema and (0,0,0) for oedema respectively (maximum score of 4) (REACH n.d.-a).

In a skin irritation test carried out with six albino rabbits, the effects observed were minimal (SCCS 2021).

Eye irritation

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

In a GLP compliant eye irritation study conducted in accordance with OECD TG 405, the chemical was instilled into 1 eye each of 4 Russian rabbits (sex unknown). The eyes were washed out after 24 hours and observed at 1, 24, 48 and 72 hours. All results at all time

points for corneal opacity, iritis, conjunctival redness and chemosis were 0. No irritation was observed in any animal (REACH n.d.-a).

Instillation of 0.1 ml undiluted substance in the eyes of six albino rabbits (Draize ţest) produced no discernible effects (SCCS 2021).

Sensitisation

Skin sensitisation

Based on the available data from non-guideline animal and human studies, the chemical is a potential skin sensitiser and hazard classification is warranted. However, the LLNA and the low incidence of cases of sensitisation in humans (despite widespread use) indicate that octocrylene is a sensitiser with low to moderate potency.

In vivo

In a guinea pig maximisation test (GPMT) conducted according to OECD TG 406, intradermal induction was performed on 10 female Dunkin-Hartley guinea pigs using 5% octocrylene in paraffin oil and topical induction with 100% of the chemical. The animals were then challenged with 100% octocrylene. Intense erythema and swelling were observed in all animals after intradermal application. Incrustation, moderate erythema and swelling in all test animals were observed after epicutaneous induction. No reactions were observed after challenge (REACH n.d.-a).

In a local lymph node assay (LLNA) performed conducted similar to OECD TG 429, CBA/Ca mice (3 per dose, sex unknown) received topical applications of 1%; 2.5%; 5%; 15%; 30% of the chemical in acetone/olive oil (4:1 v/v). The reported stimulation indices (SI) were 1.3, 1.63, 2.25, 5.01 and 4.38 for concentrations of 1%; 2.5%; 5%; 15%; 30%, respectively. The reported concentration producing a three fold increase in lymphocyte proliferation (EC3) was 7.7%, indicating moderate sensitisation potential (Karlsson et al. 2017; REACH n.d., SCCS 2021). While this study deviated from OECD guidelines (3 animals per dose, no individual scoring of animals and possible UV-irradiation from external sources) it is not considered sufficient to disregard the studies finding.

In silico

The chemical has a structural alert for protein binding based in the endpoint specific profiling functionality of the Organisation for Economic Co-operation and Development (OECD) Quantitative Structure-Activity Relationship (QSAR) Application Toolbox (OECD QSAR Toolbox). A chemical with this structural alert could interact with proteins via Michael addition on conjugated cyanoalkenes. The cyano (CN) group is not expected to be strong activator.

The QSAR modelling using OASIS-TIMES (Optimised Approach based on Structural Indices Set–Tissue Metabolism Simulator) version 2.31.2.82 (GHS model version 02.04) (OASIS LMC) predicted that the chemical was a non-sensitiser. The prediction was outside the structural domain of the model (53% in domain).

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. The alerting group is cyanoacrylate (acting as a direct hapten or an unsubstituted cyanoacrylate producing an electrophile with Schiff base forming potential).

Therefore, the chemical may interact with skin proteins by such a mechanism. The LLNA EC3 for the chemical is 7.7%, indicating moderate sensitisation potential. Note that the chemical is included in the training set and that the prediction is based on the LLNA described above (see **Skin sensitisation** – In vivo).

Observation in humans

Studies in humans indicate that contact allergy to octocrylene is rare in the general population. In patch test studies the majority of patients with allergic reactions to octocrylene had a history of photoallergic reactions to ketoprofen.

In a human repeat insult patch test (HPRIT), 205 human volunteers were treated occlusively with the chemical present at 10% concentration in lotions containing a variety of other UV filters. Octocrylene did not invoke any scores above 1 in any of the test subjects and the chemical was considered to be a non-sensitiser (REACH n.d -a).

In a European multicentre photopatch test study, 1031 patients were treated occlusively with patches containing 10% octocrylene. The patients had a history of exposed site dermatitis, reaction to a sunscreen or topical NSAID. Positive reactions attributed to Octocrylene were reported in 0.7% of test subjects (EMCPPTS 2012; REACH n.d -a).

Analysis of European patch test data generated between January 2015 and March 2016 indicated that contact allergy to octocrylene is rare. Out of the 2577 patients tested with 10% octocrylene only 0.08% had dermal reactions to octocrylene (Uter et al. 2017).

Positive sensitisation reactions to octocrylene are strongly related to a previous photoallergy to topical ketoprofen, where 27–80% of patients who were photoallergic to ketoprofen co-reacted to octocrylene. The mechanism of this reaction is unknown (SCCS 2021). Ketoprofen is not identified in any topical medicines on the (TGA n.d.).

Repeat dose toxicity

In oral studies available, reduced body weights, increased liver weights, increase in hypertrophic cells in the pituitary glands and thyroid was observed at high doses. The severity of the adverse effects or doses at which effects were observed in various organs is not sufficient to warrant hazard classification.

The lowest NOAEL reported was 175 mg/kg bw/day from a 90 day oral toxicity study. No significant toxicity was noted in dermal studies conducted. Similar effects were observed in an EOGRTS (see **Reproductive and Developmental toxicity** section) where a NOAEL of 153 mg/kg bw/day was determined.

Oral

In a GLP-compliant 90 day study conducted in accordance with OECD TG 407 Wistar rats (10/sex/dose) were administered the chemical in feed at 0, 750, 2250, 4500 and 15000 ppm or approximately 0, 53, 163, 315 and 1027 mg/kg bw/day in males and 0, 63, 187, 365 and 1143 mg/kg bw/day in females. A NOAEL of 175 mg/kg bw/day (2250 ppm) was determined from this study based on increased liver weights and increase in hypertrophic cells in the pituitary glands (REACH n.d-a).

Increased absolute and relative liver weights were observed in both sexes, with prominent acinar pattern seen in the mates of 7/10 male rats. Hypertrophy of periacinar hepatocytes and centriacar hepatocytes were observed in both sexes.

Significantly lower mean body weights were observed in males (16%) and females (15%) administered 15000 ppm octocrylene. Overall food consumption was reduced (13% and 10% for males and females respectively) in the high dose group compared to controls. Slight to moderate hypertrophy of the thyroid, follicular epitherlium and pale staining colloid was observed in both sexes.

At the highest dose a decrease in haemoglobin mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, alanine transferase and aspartate amino transferase were observed in females. An increase is platelet counts, gamma-glutamyl transferase activity and a decrease total bilirubin in both sexes was observed. Shortened prothrombin time, increase in alkaline phosphatase, total protein, globulins and total cholesterol was found in females.

In groups dosed with 4500 ppm octocrylene, an increase in plates, total protein and globulins were observed in females. A decrease in alanine aminotransferase and aspartate aminotransferase observed in females and a decrease in total bilirubin observed in both sexes. An increased number of hypertrophic cells in the pituitary glands of males was also observed in males.

Minimal changes in the thyroid gland observed in 2250 and 750 ppm dosed groups were not considered as treatment related.

In a GLP-compliant 28 day study conducted in accordance with OECD TG 407 Wistar rats (5/sex/dose) were administered the chemical (99.5% purity) in feed at 0, 1000 ppm, 3000 ppm, 10000 ppm or approximately 0, 65, 188 and 650 mg/kg bw/day in male and 0, 72, 215 and 720 mg/kg bw/day in females. The study was divided into two subsets, with Subset A and B conducted for 28 and 14 days respectively. No NOAEL was determined from this study. Significant adverse effects with an induction of liver enzymes accelerating thyroid hormone clearance in both sexes leading to higher thyroid hormone (TSH) levels and hypertrophy/hyperplasia of follicular thyroid gland cells at 10000 ppm (650 mg/kg bw/day) (REACH n.d-a; SCCS 2021).

Significantly lower mean body weights were observed in males (9.3%) and females (7.3%) administered 10000 ppm octocrylene. An increase in total white blood cell and absolute lymphocyte counts, y-glutamyl transferase, cholesterol, triglyceride and inorganic phosphate levels were observed in females. Increased TSH levels and urea levels were observed in both sexes.

At the highest dose, a significant increase of absolute and relative liver weights in males (12.85% and 23.05%, respectively) and females (21.88% and 27.20%, respectively) was observed in Subset B (14-day study). Diffuse hypertropy in livers of 1/5 males and 3/5 females. Hypertropy/hyperplasia of follicular cells in the thyroid glands of 2/5 females and 3/5 females were also noted.

In animals dosed at 10000 ppm of the chemical in Subset B (14 day study), induction of liver enzymes (PROD, BROD, T4-specific UDP glucuronosyltransferase) was observed, accelerating the thyroid hormone clearance. This created a compensating positive feedback mechanism leading to higher TSH levels and hypertrophy/hyperplasia of follicular thyroid gland cells. These effects were not observed at doses of 1000ppm or 3000ppm.

In a 14 day oral toxicity study, Wistar rats (3/sex/dose) were administered the chemical in feed at 4500 and 15000 ppm or 456, 1369 mg/kg bw/day in males and 449, 1393 mg/kg bw/day in females. No mortality or adverse clinical effects were observed during the study. A slight decrease in body weights was observed (3% males, 7% females) in animals dosed with 15000 ppm of the chemical. Due to the small effect and low number of test animals a NOAEL was not determined from this study.

Dermal

In a 90 day dermal toxicity study, NZW rabbits (5/sex/dose) were administered the chemical by dermal application at 0, 130, 264 and 534 mg/kg bw/day in 80% (w/w) petrolatum and 20% (w/w) C12-15 alkylbenzoate (Finsolv), 5 days/week.

No adverse effects were observed in any of the animals included in the study besides minor histopathological effects near the site of application. These effects included greater incidence of skin abnormalities such as erythema and desquamation than control animals.

In both sexes at concentrations above 264 mg/kg bw/day, significantly depressed body weight gain relative to controls was observed. No decrease in body weight was observed at 130 mg/kg bw/day in females.

Absolute liver weight of males was reduced at all octocrylene dose levels, but these effects were relative to the overall reduction in body weights. Liver weights in females were unchanged at all dose levels: however, with an increase in the organ to body weight ratio at 264 and 534 mg/kg bw/day.

No macroscopic or histopathological abnormalities in any organs examined were observed. Similarly, all clinical hematology values were within the historical control limits. In male rabbits, no effects were observed on the epididymis and testes at any dose level.

Inhalation

No data are available.

Observation in humans

Genotoxicity

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

In vitro

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 (REACH n.d.-a).

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 1535 and TA 1537 with and without metabolic activation at concentrations up to 10000 µg/plate (REACH n.d.-a).

- Reverse mutation assays (OECD TG 471) in *Escherichia (E.) coli* WP2 uvr A with and without metabolic activation at concentrations up to 2500 µg/plate in the presence of UV light (REACH n.d.-a).
- Mammalian cell gene mutation assay (OECD TG 476) in mouse lymphoma L5178Y $T/K^{+/-}$ cells with and without metabolic activation up to 200 µg/mL (REACH n.d-a)
- Multiple in vitro Mammalian Chromosome Aberration Test (OECD TG 473) in Chinese hamster lung fibroblasts (V79) with and without metabolic activation up to 100 µg/mL (REACH n.d-a).

In vivo

Negative results were reported in the following a Mammalian Erythrocyte Micronucleus Test (OECD TG 474) in NMRI mice (5/sex/dose) at 500, 1000 and 2000 mg/kg bw (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 chemical and its 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.

There is sufficient evidence that the impurity/breakdown product benzophenone has carcinogenic effects in animals based on the observation of benign and malignant neoplastic lesions in the liver and kidneys in both sexes of mice and rats. Effects in these organs were seen consistently across repeated dose studies, reproductive toxicity and carcinogenicity studies with statistically significant increased incidence reported for histiocytic sarcoma at 70 mg/kg bw/d in female mice. The mode of action is uncertain, and the available data supports a likely threshold mode of action (AICIS 2025).

Reproductive and development toxicity

Based on the available data, the chemical may cause adverse effects on fertility warranting classification. A reduced number of implantation sites and lower number of pups delivered were observed in an EOGRTS and range finding study. The effects were observed only in the high dose groups together with mild systemic toxicity in dams. There was no evidence of specific developmental effects in the available studies. The available data warrant hazard classification.

Sexual function and fertility

In a GLP compliant EOGRTS conducted in accordance with OECD TG 443, Wistar rats (12/sex/dose) were administered the chemical in feed once daily at, 750, 2100, 7000 ppm (equivalent to 55 mg/kg bw/d males and 58 mg/kg bw/d females, 153 mg/kg bw/d males and 163 mg/kg bw/d females,
534 mg/kg bw/d males and 550 mg/kg bw/d females, respectively) for 10 weeks in the premating period through to the postnatal day (PND) 21. At weaning, pups were distributed to different cohorts and were exposed to the same dose levels of the test substance as their parents during their growth into adulthood. Cohorts 1A and 1B of this study assessed reproductive performance and Cohorts 2A and 2B focused on neurodevelopmental endpoints. Animals of Cohort 1B were used for breeding a second generation.

The following exposure periods applied:

- F0 males: 10-week premating period, during mating up to the day of sacrifice (approx. 13 weeks)
- F0 females: 10-week premating period, during mating, gestation and lactation up to the day of sacrifice after lactation day 21 (approx. 18 weeks)
- F1: from weaning up to sacrifice
    - approx.10 weeks in cohort 1A, approx.
    - approx. 13 weeks (males) and approx. 18 weeks (females) in cohort 1B
    - approx. 8 weeks in cohort 2A)
- F2: indirectly exposed until weaning.

Measures of general systemic toxicity were examined in the in the F0-cohort and F1 -generation cohort 1A. The following effects were observed in animals treated with 7000 ppm octocrylene:

- increased relative liver (males ~20%, females ~30%) and thyroid weight (males ~25 to 30%, females ~25%)
- higher thyroid weight accompanied by an increased incidence of activated appearance, characterised by the loss of colloid from the follicles and hypertrophy and hyperplasia of follicular epithelial cells
- lower body weights were observed in males and females (during premating: F0 males 7%, F0 females 11%; F0 females during gestation 13%, F0-females during lactation 11% and F1-Cohort 1A males 8%, females 14%).

Food consumption was also statistically significantly lower than control animals (F0-Cohort 10% in males and 19% in females and in F1-Cohort 1A 6% in males and 13% in females). No treatment related effects were observed on parameters related to the oestrus cycle in the F0-generation or in animals of Cohort 1A of the F1-generation. No treatment related effects were observed on epididymal and testicular sperm parameters in the F0-generation or in animals of Cohort 1A of the F1-generation (SCCS 2021).

In animals treated with 7000 ppm octocrylene, decreased implantation and litter sizes were observed in the F0-generation and Cohort 1B of the F1- generation. In the F0-generation a lower mean number of implantation sites (10.7 versus 12.3 in controls) and a lower number of pups delivered (9.6 versus 11.4 in controls) were observed. In the Cohort 1B of the F1- generation the lower mean number of implantation sites (9.3 versus 10.7 in controls) and a lower number of pups delivered (9.3 versus 10.3) were observed. No other relevant effects on fertility were observed.

In a GLP compliant dose range finding study for Extended One Generation Reproductive Toxicity Study (EOGRTS), conducted in accordance with the REACH regulation (EC) No 1907/2006, similar effects were observed to the full EOGRTS. Fewer implantation sites and pups were observed at the high dose of 15000 ppm (equivalent to 812-1271 mg/kg bw/day for males and 796-1740 mg/kg bw/day for females) with both birth weight and postnatal body weight development decreased. No other treatment related mortality or other treatment related clinical effects were observed (SCCS 2021).

Development

In a percutaneous developmental toxicity study, NZW rabbits (17/females/dose) were administered the chemical by dermal application in a mixture of petroleum and C1-15 alkylbenzoate at 0, 65 and 267 mg/kg/day on GD 6-18 (SCCS 2021).

No observable difference in body weights, food consumption and further maternal parameters including clinical observations and gross necropsy of thoracic and abdominal viscera, uterus and ovaries between treated and control animals. No treatment related effects were observed in mortality, survival rates, gender ratios, litter sizes and weights, including external, soft tissue, skeletal and head examinations.

In an in vivo teratology screening study, CD-1 mice (12/females/dose) were administered the chemical by oral gavage in corn oil at 0, 100, 300 and 1000 mg/kg bw/day on GD 8-12 (SCCS 2021).

No decrease in offspring delivery and maternal body weight changes were observed at any of the doses. Reduced pregnancy rates observed at 1000 mg/kg bw/day was not attributable to the test substance, which was administered after mating. No differences between litter size and number of live and dead pups delivered was observed between the test groups.

In the EOGRTS (see **Reproductive and Developmental Toxicity** section), no treatment related effects were observed on post-implantation loss, stillborn pups, dead, missing and/or cannibalized pups, pup viability indices, sex ratio, clinical signs of pups nor on macroscopic observations at sacrifice in F1 and F2 pups. In the high-dose group, the body weight of F1 and F2 pups was decreased (-10%) on PND 21. Decreased body weight in F1 pups weight was observed from PND 14 (beginning of solid diet). Decreased body weight in F2 pups was observed from PND 4 (before solid diet). At the highest dose level, F0 and F1 females' body weights were 11% and 9% lower compared to controls at the start of lactation (SCCS 2021).

In the EOGRTS (see **Reproductive and Developmental Toxicity** section), no neurological treatment related abnormalities were observed in animals of Cohort 2A of the F1-generation. No adverse effects were observed on brain weight, brain length and brain width in animals of Cohort 2A or Cohort 2B or from brain morphometric analysis. Macroscopic observations at sacrifice of animals including neuronal tissues in these cohorts did not reveal any treatment related abnormalities (SCCS 2021).

There were no effects of the test item on neuro (developmental) parameters. The NOAEL for neuro (developmental) parameters was placed at the high dose concentration of 7000 mg/kg diet (534 mg/kg bw/day for males and 550 mg/kg bw/day for females) (SCCS 2021; REACH n.d -a). Several limitations in the reliability of the study was noted by the Regulatory Management Option Analysis (RMOA), including inappropriate statistical analysis, absence of historical controls and positive controls, poor method reporting and absence of raw data for auditory startle response. The low reliability of the study hampers the ability to draw conclusions (ECHA 2023).

In the high dose group preputial separation, vaginal opening and first oestrus stage occurred later in Cohort 1A generation offspring. However, these differences were considered a consequence of delayed general development stemming from lower pup weights. No direct treatment related effects were observed on organ weights, nipple retention (male F1-generation pups or Cohort 1B F2-generation pups), development of the ovarian follicles from primordial small follicles into corpora lutea or splenic lymphocyte subpopulation analysis in Cohort 1A F1-generation animals (SCCS 2021).

In a GLP compliant prenatal developmental toxicity study conducted in accordance with OECD TG 414, pregnant Wistar rats (25/dose) were administered the chemical by gavage once daily at 100, 400 and 1000 mg/kg bw/day on gestational days (GD) 6-15. Dams were sacrificed on GD 20 and the foetuses examined. No mortalities were observed in any of the groups and no mean differences in food consumption, body weight, uterus weight, conception rate, corpora lutea, implantation sites or losses, resorptions or viable foetuses. Higher absolute and relative liver weights (9%) were observed in animals dosed at 1000 mg/kg bw/day. This trend was also observed in groups dosed with 400 mg/kg bw/day with increased liver weights (6%) compared to controls. The maternal observed adverse effect level (NOAEL) was 100 mg/kg bw/day based on increased liver weights and the lowest adverse effect level for foetal effects based on no differences between treated and control groups was 1000 mg/kg bw/day (REACH n.d-a).

A potential metabolite of octocrylene is 2-ethylhexanol (see **Toxicokinetics** section) which classified for reproductive toxicity – category 2. Effects from this metabolite were not observed in any studies indicating that 2-ethylhexanol may not be bioavailable systemically at doses that are high enough to be toxicologically relevant.

Endocrine effects

Octocrylene is listed on the Endocrine Active Substances Information System (EASIS n.d.). There is evidence that octocrylene interacts with endocrine system; however, 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 (SCCS 2021). Based on the available information, the chemical may interfere with the thyroid hormone system although effects were not observed consistently across studies. The observed effects may be mediated by changes to the thyroidal signalling as a result of liver enzymatic induction.

Oestrogenic, androgenic and steroidogenesis (EAS) effects

In vitro

The chemical was reported to havenegative results in (ECHA 2023):

- 2 oestrogen yeast transactivation assays
- 5 out of 5 assays investigating oestrogen agonism in TOX21 battery.

Mixed results were observed in assays (ECHA 2023):

- with slight androgenic activity in a yeast transactivation assays
- negative in another yeast transactivation assay
- negative in 3 out of 3 assays investigating androgen agonism in TOX21 battery
- positive in 2 out of 3 assays investigating androgen antagonism in TOX21 battery.

The following available in vitro studies showed mixed results in steroid activity (ECHA 2023):

- increased progesterone and slightly decreased corticosteroids and adrenal androgens in H295R cells
- slightly inhibited aromatase activity in TOX21 battery.

In an uterotrophic assay in immature female Wistar rats, the chemical did not induce histopathological and organ weight increase in the uterus up to 1000 mg/kg bw/day. Based on the uterotrophic assay results, the chemical does not have oestrogenic effects in rats (ECHA 2023).

In a Hershberger assay in male Wistar rats, the chemical induced significant decrease (~20%) of absolute and relative weights of the ventral prostate and levator ani plus bulbocavernosus muscles. Although decreased weights (~10%) were observed in three other tissues, i.e. the seminal vesicle, glans penis and Cowper's glands, these were not statistically significant. Furthermore, levels of testosterone, dihydrotestosterone and luteinising hormone were not affected. Given that there were no histopathological effects observed in the prostate, seminal vesicle and bulbourethral gland in the treated animals to correlate with the decreased weights of these tissues, the decreased weight may have been a random variable. Alternatively, the decreased weights in these tissues could be attributed to enzyme induction based on the observed increased liver weights related to a higher metabolism rate of the substituted androgen testosterone propionate. Taken together, the chemical does not have antiandrogenic effects in rats (ECHA 2023; SCCS 2021).

In the EOGRTS (see **Reproductive and Developmental toxicity** section), there were no changes in

- weights and histopathology of male and female reproductive organs
- sperm parameters
- corpora lutea
- follicles
- oestrous cyclicity
- anogenital distance.

The decreased number of implantation sites in the high dose females in the EOGRTS and EOGRTS dose range finding study is not sufficient evidence that the chemical has caused the adverse effect mediated by an EAS activity (ECHA 2023; SCCS 2021).

Thyroid effects

In vitro

No specific in vitro studies have been undertaken. There were some signs of endocrine activity relevant for thyroid effects in toxcast assays; however, most effects occurred at cytotoxic concentrations (SCCS 2021).

In vivo

In a GLP-compliant mechanistic study similar to OECD TG 407, (see **Repeated dose toxicity** section) there was an increase in thyroid stimulating hormone (TSH) level in both sexes in the high dose group (630-720 mg/kg bw/day,) after 14 and 28 days. There was a decrease (not statistically significant) in T4 level at different time points in the high dose group (ECHA 2023). In this study the chemical induced changes in the activity of a number of

enzymes, suggesting that the thyroidal activity of the chemical may be mediated via liver enzyme induction.

The EOGRTS did not show similar changes in TSH and T4 levels. However, in this study there was a high interindividual variability in TSH measurements controls. TSH measurements were only done at sacrifice and the highest dose tested was lower (534 mg/kg bw/day for males and 550 mg/kg bw/day for females). A decrease in T4 level (not statistically significant) was observed in PND4 pups in the high dose group in the F1 (25%) and F2 (33%) generations. However, the low number of high dose culled pups due to the high preimplantation loss reduced the reliability of this result (ECHA 2023).

Across several in vivo studies including the rat mechanistic study and the EOGRTS, consistent findings of thyroid follicular hypertrophy and/or hyperplasia and pale staining colloid was reported from 2100 ppm (153–163 mg/kg bw/day) in the EOGRTS up to the highest dose tested (15000ppm; 1027–1143 mg/kg) in the 90 day study. In addition, relative thyroid to body weight was increased (25–30% in F0 (both sexes) and F1 males) at 7000 ppm (534 mg/kg bw/day for males and 550 mg/kg bw/day for females) in the EOGRTS. Common findings also include relative liver to body weight increase across the in vivo studies, as well as diffuse hypertrophy in the liver (ECHA 2023).

In high dose groups of the EOGRTS and EOGRTS dose range finding studies, decreased number of implantation sites and hypertrophic cells in the pituitary gland (males) were observed in the presence of general toxicity (ECHA 2023). These effects may have been a direct or indirect result of changes in thyroid signalling but there is insufficient data to rule out other modes of action.

Observations in humans

In a Chinese epidemiological study, no association between the chemical urinary levels and polycystic ovarian syndrome (PCOS) was observed. There was a positive association between the chemical and PCOS risk in obese and overweight women (body mass index (BMI >24). This single case control study only had a limited number of cases and; therefore, a conclusion cannot be made (ECHA 2023).

Human sperm parameters such as sperm acrosome reaction, sperm penetration, the proportion of hyperactivated sperm cells and sperm viability were not altered when exposed to 10 µM octocrylene in vitro (ECHA 2023; SCCS 2021).

Human health risk characterisation

Critical health effects

The critical health effects for risk characterisation are systemic effects including effects on reproduction.

A NOAEL of 153 mg/kg bw/day was determined for the above OECD TG 443 (see **Reproductive Toxicity**). The SCCS previously estimated the NOAEL for this study to be 76.5 mg/kg bw/day. This estimation was derived by applying an assessment factor of 2 to account for 50% oral bioavailability.

In the absence of other information, the NOAEL of 76.5 mg/kg bw/day was used for risk characterisation.

Public risk

Exposure to octocrylene

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.

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, an MOE 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 octocrylene 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 3 – Margin of exposure (MOE) values for octocrylene in cosmetic products at maximum concentrations.

Product type	NOAEL (mg/kg bw/day)	Daily systemic exposure (mg/kg bw/day)	Margin of exposure (MoE)
Face cream	76.5	0.020	3,825
Fine fragrances	76.5	0.006	12,750
Hand cream	76.5	0.028	2,732
Lipstick, lip balm	76.5	0.045	1,700
Liquid foundation	76.5	0.018	4,250
Body lotion	76.5	0.507	151
Aggregate exposure (all products)	-	**0.695**	**110**

Based on the worst case scenario estimates when octocrylene is used in all products at 10% concentration, an MOE of 110 is calculated (see **Table 3**). This indicates that octocrylene is unlikely to pose a risk to human health if used in cosmetic products at concentrations of 10% or less.

Exposure to benzophenone

Based on the worst case scenario estimates from products containing octocrylene, the aggregate systemic exposure to the chemical as an impurity/breakdown product is 0.013 mg/kg bw/day. This estimate is approximately a third of the TDI recommended by EFSA. EFSA considered this TDI sufficiently protective for the non-neoplastic effects in repeat dose toxicity studies and the neoplastic effects in the carcinogenicity studies (AICIS 2025).

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