Australian Government
Department of Health, Disability and Ageing
Australian Industrial Chemicals Introduction Scheme

Methanone, diphenyl- (Benzophenone)

Evaluation statement (EVA00184)

26 June 2025

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AICIS Evaluation statement (EVA00184)

Subject of the evaluation

Methanone, diphenyl- (Benzophenone)

Chemical in this evaluation

Name	CAS registry number
Methanone, diphenyl-	119-61-9

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 methanone, diphenyl- (benzophenone).

Benzophenone was previously assessed, including all endpoints, under the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework, under the former National Industrial Chemicals Introduction and Assessment Scheme (NICNAS). New information has become available regarding carcinogenicity, exposure and potential public health risks. The chemical has also been identified as both an impurity and breakdown product in products containing octocrylene. Octocrylene is being assessed concurrently (AICIS 2025). Therefore, this evaluation will:

- review the weight of evidence including new information on carcinogenicity
- undertake a quantitative risk assessment to estimate potential public risks related to the chemical including as an impurity/degradation product in products containing octocrylene
- consider whether current regulatory controls are sufficient to prevent significant risks to the public and workers.

The risk of benzophenone in food and as an impurity/degradation product in therapeutic sunscreens is not assessed in this evaluation because these are not industrial uses.

Summary of evaluation

Summary of introduction, use and end use

In Australia, benzophenone has recently been reported to be used in printing inks at concentrations ranging 4.8–5.2%.

The global use of the chemical is expected to be declining due to regulatory action in some jurisdictions. However, available use information suggests that the chemical is still being introduced in Australia. The Australian use volume of benzophenone in 2023 was estimated to be 1000 kg/year based on data collected in the Asia-Pacific region by the International Fragrance Association (IFRA).

Based on international information, the chemical has reported uses in:

- personal care products (cosmetics) with identified functional uses as a fragrance ingredient and light stabiliser
- domestic products including paint and coating products, cleaning and furniture care products and air care products (including scented candles)
- commercial products including paints and coating products
- site limited application with functional use as an intermediate and as a UV stabiliser.

There is limited information on use concentrations of the chemical. Historically the chemical was used at 0.3% in personal care products and paint and stains, up to 5% in nail polish and up to 10% in fragrances (although typical concentrations are < 3%). While the chemical may be used in a diverse range of personal care products (cosmetics), the available information does not suggest it has widespread cosmetic use based on low reported use frequencies.

The chemical is both an impurity and degradation product of octocrylene (CAS No. 6197-30-4), which is a chemical that is used in a range of personal care products (cosmetics).

The chemical has non-industrial uses in food products.

Human health

Summary of health hazards

The identified health hazards are based on available data for the chemical. The chemical can be absorbed following oral and dermal exposure. No absorption data are available for inhalation exposure, but it is expected to be bioavailable. The metabolites of benzophenone following oral exposure in laboratory animals were determined to be benzhydrol and 4-hydroxybenzophenone.

Based on the previously assessed data (NICNAS 2015), the chemical:

- has low acute oral and dermal toxicity
- may be slightly irritating to the skin and eyes
- is not sensitising to skin up to concentrations of 10%
- is not expected to have genotoxic potential based on *in vitro* and *in vivo* assays
- Is not expected to cause specific reproductive or developmental toxicity.

Maternal toxicity including reduced maternal bodyweight was reported in a number of developmental toxicity studies. The lowest no observed adverse effect level (NOAEL) reported was 5 mg/kg bw/day. This value has been considered in this evaluation for determining risk from acute exposures.

Information on carcinogenicity including consideration of repeated dose toxicity and endocrine activity has been reviewed as part of this evaluation.

There is sufficient evidence that the chemical has carcinogenic effects in animals. The chemical caused:

- benign and malignant tumours in several organ systems including increased incidences of the rare tumours histiocytic sarcoma (in female rats and mice) and hepatoblastoma (in male mice)
- other neoplastic and non-neoplastic effects in the liver, kidneys, and haematopoietic system including the spleen.

The mode of action for carcinogenicity has not been established. However, the available data including consideration of genotoxicity and endocrine activity supports a likely threshold mode of action.

Effects in the liver and kidney were seen consistently across repeated dose studies, reproductive toxicity and carcinogenicity studies. Internationally, kidney effects were identified as the most sensitive endpoint for assessing the risks of long term exposure to the chemical. A tolerable daily intake (TDI) of 0.03 mg/kg bw/day was set by the European Food Safety Authority (EFSA) based on kidney effects. This TDI value is considered to be sufficiently protective for both the non-neoplastic effects in repeated dose toxicity studies and the neoplastic effects in the carcinogenicity studies.

Hazard classifications relevant for worker health and safety

The chemical satisfies the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) for hazard classes relevant for work health and safety as follows. This is an amendment to the current classification for carcinogenicity on the Hazardous Chemicals Information System (HCIS) (see **Supporting information**). This does not consider classification of physical hazards and environmental hazards.

Health hazards	Hazard category	Hazard statement
Carcinogenicity	Carc. 1B	H350: May cause cancer

Summary of health risk

Public

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

- by direct application of personal care products to the skin at concentrations up to 3%
- by incidental dermal contact and inhalation when using nail products at concentrations up to 5%
- by incidental dermal contact and/or inhalation from use of domestic products including scented candles, cleaning sprays and paints and stains
- through use of products containing octocrylene due to its presence both as an impurity and degradation product.

For repeated frequent exposures to the chemical, the TDI of 0.03 mg/kg bw/day was considered to be appropriate for assessing risk. This is considered to be sufficiently protective for the non-neoplastic effects in repeat dose toxicity studies and the neoplastic effects in the carcinogenicity studies.

A comparison of estimated exposures, from a range of personal care products and domestic products that may be used daily, was compared with the TDI to estimate risks. The majority of products (if considered individually) resulted in estimates that were < 50% of the TDI. However, exposure estimates indicated that use of body lotions containing 0.3% of the chemical and fine fragrances containing 3% of the chemical would exceed the TDI. This indicates that these products may pose a health risk to the public if used repeatedly over time. In addition, the exposure estimates indicated that frequent use of scented candles containing the chemical at 0.3% concentration would provide exposures similar to the TDI.

Based on the worst case scenario estimates from products containing octocrylene, the aggregate systemic exposure to the chemical as an impurity or degradation product was estimated to be approximately 45% of the TDI. The daily systemic exposure to the chemical from products that have not aged significantly would be approximately an order of magnitude lower than the estimate.

There may be additional single exposures to the chemical from infrequently used domestic products such as paints and stains. For these acute exposures, the lowest NOAEL of 5 mg/kg bw/day established in a developmental toxicity study in rabbits was considered to be relevant for public health risk. A margin of exposure (MOE) methodology was used to characterise the risk to human health from acute infrequent exposures. The worst case scenario exposure estimates for these acute exposures all had MOE values greater than 100. The MOE value estimates the likelihood that an adverse health effect will occur under the conditions of exposure. Using interspecies and intraspecies assessment factors of 10, the acceptable MOE for an NOAEL based assessment is greater than or equal to 100. This indicates that there is a low risk of health effects to the public from these short term exposures.

Overall, given the identified potential long term systemic health hazards, the evidence indicates that there is a risk to the public following repeated, long term exposure to the chemical that requires management (see **Proposed means for managing risks** section). The individual use of certain products results in exposures at the level of or exceeding the TDI. Although available data indicates that it is unlikely that an individual has daily exposure to multiple personal care products containing the chemical as an ingredient, aggregate exposures to personal care products containing the chemical as an ingredient and octocrylene as an ingredient cannot be ruled out. In addition, aggregate exposures could result from use of domestic products. The risk could be managed by including benzophenone in an appropriate schedule of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP).

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 cleaning and maintaining equipment.

Worker exposure to these chemicals at lower concentrations could also occur while using formulated products containing these chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic long term health effects, these chemicals could pose a risk to workers. Control measures to minimise dermal, ocular and inhalation exposure are needed to manage the risk to workers (refer to **Proposed means of managing risk**).

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 Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP).

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

- restricts the chemical concentration.

Consideration should be given to the following:

- The chemical is carcinogenic with a threshold mode of action.
- The chemical may be used as an ingredient in a wide range of personal care (cosmetic) and domestic products.
- The chemical is restricted or prohibited for cosmetic use overseas. Although the global use of the chemical is expected to be declining due to regulatory action in some jurisdictions, available use information suggests that the chemical is still used in Australia.
- The individual use of certain products (body lotion, fine fragrance and scented candles) results in exposures at the level of or exceeding the TDI.
- The public could be exposed to benzophenone as both an ingredient and as a breakdown product in consumer goods containing octocrylene. Although available data indicates that it is unlikely that an individual has daily exposure to multiple personal care products (cosmetics) containing the chemical as an ingredient, aggregate exposures to personal care products containing the chemical as an ingredient and octocrylene as an ingredient cannot be ruled out. In addition, aggregate exposures could result from use of domestic products.
- The public is also exposed to benzophenone through non-industrial uses in both food and as an impurity/degradation product in therapeutic sunscreens.
- Given that the public may be exposed to a diverse number of products with varied exposure estimates and hence contribution towards aggregate exposure, it is not possible to recommend a definitive concentration limit that should be applied to all products.
- However, we note that:
    - A concentration limit of 0.1% would reduce exposures from use of body lotion, which is the highest potential contributor to exposure to 50% of the TDI.
    - Exposure to rinse-off personal care products and domestic products (except scented candles) results in lower exposures compared to leave-on personal care products.
    - The exposure estimate for scented candles is based on a scenario where a user burns candles almost every day. The exposure estimate for users who only use candles infrequently would be significantly lower.

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.

Information relating to safe introduction and use

The information in this statement including recommended hazard classifications, should be used by a person conducting a business or undertaking (PCBU) 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 oral, dermal and inhalation exposure to the chemical 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 chemical.

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.

Measures required to eliminate, or manage risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is 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 Safe Work Australia 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

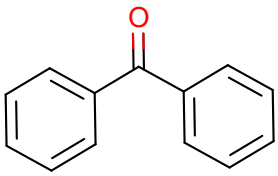
The Executive Director is satisfied that the identified risks to human health from the introduction and use of the industrial chemical can be managed.

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	119-61-9
CAS name	Methanone, diphenyl-
Molecular formula	$C_{13}H_{10}O$
Associated names	Benzophenone
	Benzoylbenzene
	Diphenyl ketone
	Diphenylmethanone
Molecular weight (g/mol)	182.22
SMILES (canonical)	O=C(C=1C=CC=CC1)C=2C=CC=CC2
Structural formula	

Relevant physical and chemical properties

Physical form	solid
Melting point	48.5°C
Boiling point	305.4°C
Vapour pressure	0.257 Pa at 25°C
Water solubility	23.9 mg/L
log K_{ow}	3.2

Source: REACH n.d.-a

Introduction and use

Australia

Recent information provided to AICIS as part of this evaluation, indicates use of the chemical in printing inks at concentrations ranging 4.8–5.2%.

The Australian use volumes of benzophenone as a fragrance were estimated to be 850 kg/year in 2019 and 1000 kg/year in 2023, based on data collected in the Asia-Pacific region by the International Fragrance Association (IFRA).

The chemical has non-industrial uses in therapeutic goods (TGA 2024).

International

The chemical is registered under the Registration, Evaluation Authorisation and Restriction of chemicals (REACH) regulation and is manufactured in and/or imported to the European Economic Area, at more than 1000 tonnes per annum (REACH n.d.-a). In 2008, less than 1000 kg of benzophenone were reported to be manufactured in Canada and 35,000 to 135,000 kg were reported to be imported into Canada (Government of Canada 2021). The chemical was considered to be a high-volume chemical by the United States Environmental Protection Agency (US EPA) with a volume of 453,000 kg in 2003 (IARC 2013; NTP 2006). The chemical occurs naturally in the environment (in a limited number of fruits and plants) and is also synthetically manufactured (IARC 2013).

The following uses were identified from: Danish EPA 2015; Government of Canada 2021; IARC 2013; INCI beauty n.d.; De Lima Associates n.d.; EWG n.d; Personal Care Products Council n.d.; Perfumers world n.d.; REACH n.d.-a; US CDR 2016; US CDR 2020.

The chemical has reported cosmetic uses in personal care products including:

- fragrances
- body lotion
- face cream
- hand cream
- makeup
- deodorant
- nail products
- hair products
- body wash.

The reported functions of the chemical in personal care products are as a fragrance and a light stabiliser (CosING n.d.; Personal Care Products Council n.d.). The chemical is listed on the IFRA transparency list, a list of ingredients used by fragrance companies around the world (IFRA n.d.).

While the chemical may be used in a wide range of products, the available information does not suggest it has widespread cosmetic use. The chemical was identified in:

- 0.04% of all cosmetic products including fragrances, deodorants (spray) and hair products (non-spray) according to the INCI beauty website (INCI beauty n.d)

- 232 (0.2% of reported products) products sold on the US market (Johnson et al. 2023)
- 4 products including face cream and hair conditioners according to the Consumer Product Information Database (CPID) in the United States (US) (DeLima Associates n.d.)
- 9 products according to the Voluntary Cosmetics Registration Program (VCRP) in the US (Personal Care Products Council 2011)
- 6 products including body lotion, hand cream and nail products according to the EWG skin deep website (EWG n.d.)
- 0 products in an industry survey performed by the Danish Environmental Protection Agency from October 2013 to August 2015 (Danish EPA 2015).

There is limited information on the concentrations of the chemical in personal care products. Historically, the chemical has been used at concentrations of up to:

- 0.3% in fragrance, body cleanser (Government of Canada 2021)
- 0.15% in soap (NTP 1991)
- 0.015% in creams (NTP 1991)
- 5% in nail polish (Government of Canada 2021).

It is sold online as an ingredient for perfumery (typically at 10% concentration). Typical use in fragrances have been reported to be 3.0% (average concentration) and 10% (max concentration) (Perfumer's World n.d.).

The chemical has been detected in sunscreens containing octocrylene (CAS No. 6197-30-4) (see **Human exposure**). The chemical is a known degradation product of octocrylene and may also be present as an impurity from octocrylene synthesis. Therefore, the chemical may be present in cosmetic products which also contain octocrylene (AICIS 2025).

Based on information from the CPID, the chemical has reported domestic uses in the US in:

- cleaning products
- air care products, particularly scented candles
- paint and coating products, including indoor paints and stains for wood surfaces
- furniture care products.

The concentrations of the chemical in interior paints and exterior wood stains were less than 0.2% and 0.3% respectively. No other concentrations for domestic products were reported (DeLima Associates n.d.).

The chemical has reported commercial uses in:

- cleaning products
- paints and stains
- automotive care products, including waxes and leather conditioning wipes
- anti-freeze products
- adhesives and sealants
- inks and toners.

The chemical has reported site limited uses as a photoinitiator. The chemical may also be added to plastic packaging or contents to prevent the UV photo-degradation of packaging plastics or its contents (IARC 2013).

The chemical has non-industrial uses as a flavouring additive in foods.

Existing Australian regulatory controls

AICIS

No specific controls are currently available for the chemical.

The chemical is listed on the Australian Industrial Chemicals Introduction Scheme (AICIS) − List of chemicals with high hazards for categorisation.

Public

No specific public controls have been identified for industrial uses of the chemical

Non-industrial: The chemical is a specified permissible ingredient (TGA 2025). The following requirements apply to the chemical when contained in a medicine:

- Permitted for topical use only in combination with other permitted ingredients as a fragrance.
- The total concentration of fragrance proprietary excipient formulations containing benzophenone must not be more than 1% of the total medicine.

The chemical is excluded from the list of sunscreen agents permitted as active ingredients in listed products sold domestically (TGA 2023).

Workers

The chemical is listed on the Hazardous Chemical Information (HCIS) with the following hazard categories and statements for human health (SWA n.d.):

Health hazards	Hazard category	Hazard statement
Carcinogenicity	Carc. 2	H351: Suspected of causing cancer

International regulatory status

Exposure standards

The following exposure standards were identified (Chemwatch n.d.):

- an exposure limit of 0.5 mg/m^3 time weighted average (TWA) in the United States of America and a limit of 2 mg/m^3 in Russia.

Canada

The chemical is listed on the Health Canada Cosmetic Ingredient Hotlist - List of Ingredients that are Restricted for Use in Cosmetic Products, with a maximum concentration permitted of 3% (Government of Canada 2025).

The Government of Canada has published a “Risk management approach for benzophenone”, with the following proposed risk management actions to address human health concerns (Government of Canada 2021):

1. “Measures to reduce exposures to benzophenone from certain cosmetics by describing benzophenone as prohibited or restricted ingredients on the Health Canada Cosmetic Ingredient Hotlist”
2. “A measure to reduce the concentrations of benzophenone to a maximum of 0.1 % (w/w) or 1000 mg/kg in certain exterior and interior paint, stain and/or coating products that are available to consumers in Canada.”

European Union

The chemical is listed on ‘EU Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 - Annex II - List of Substances Prohibited in Cosmetic Products’ (EC n.d.).

Benzophenone as an impurity and/or degradation product of octocrylene shall be kept at trace level (EC n.d.).

The EFSA derived a TDI of 0.03 mg/kg bw for benzophenone to cover the non-neoplastic effects in the chronic toxicity studies and the neoplastic effects induced in the rodent carcinogenicity studies (EFSA 2017).

New Zealand

Benzophenone as an impurity and/or degradation product of octocrylene shall be kept at trace level (NZ EPA 2024).

United States of America

Synthetic benzophenone is banned as a food additive and as a plasticiser in rubber articles intended for repeated use in contact with food (FDA 2018).

Asia

The chemical is included as a footnote to the octocrylene listing on the Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex VII - List of UV filters which cosmetic products may contain. Benzophenone as an impurity and/or degradation product of octocrylene shall be kept at trace level (HSA 2024).

Human exposure

Public

Previous public exposure estimates by other international agencies have focused on specific product types and used different assumptions about the concentration of benzophenone in these products. Health Canada previously estimated systemic exposure to the chemical from consumer use of cosmetic and domestic products that were identified in a survey and based on reports under their legislation (Government of Canada 2021). They assumed that the main cosmetic uses of the chemical were in nail polishes, fragrances, body cleansers,

makeup, and hair products at concentrations up to 0.3%, except in nail polish when a concentration of 5% was used. Whilst there were no specific reports of the use of the chemical in cosmetic products in a survey, the Danish EPA noted that the chemical may be used in fragrances. They estimated the worst case systemic exposure to the chemical from use of fine fragrances with an assumed chemical concentration of 1% (Danish EPA 2015).

These international estimates did not account for all potential sources of benzophenone identified in this evaluation (see **Introduction and use**). In addition, new information on the dermal absorption of the chemical through human skin is available (see **Toxicokinetics**). The dermal route is a significant route of exposure to the chemical based on previous estimates.

The public exposure to the chemical in adults was estimated for scenarios relating to its use in personal care (cosmetic) and domestic products. In this exposure assessment, the reasonable worst case approach is used, in which estimates are based on worst case, but plausible, exposure scenarios. For the exposure assessment, the use amounts were determined based on values established by the EU Scientific Committee on Consumer Safety (SCCS 2023) and Netherlands National Institute for Public Health and the Environment (RIVM 2006).

A dermal absorption value of 12.42% was used, based on the available *ex vivo* human skin study (Ejaz et al. 2024). In the absence of specific data, the default inhalation absorption value was assumed to be 100%. Oral exposures were not considered in the following estimates. A default adult body weight of 60 kg was assumed for all scenarios.

Chronic exposures – frequently used products

Personal care products (cosmetics) containing benzophenone are expected to be used daily. Depending on the type of product, dermal contact with personal care products can be limited to specific areas of 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.

For these products, the dermal route is the most significant route of exposure. Estimates of inhalation exposure to the chemical from these personal care products are orders of magnitude lower than the dermal estimates and; therefore, only the dermal estimates are presented. The concentration of the chemical in these products was assumed to be 0.3%. The exceptions were in fine fragrances where concentrations were assumed to be 3.0% and in nail polish where concentrations were assumed to be 5.0% based on values reported internationally (see **Introduction and use** section). The daily systemic dermal exposure to these products was estimated and the values are presented in **Table 1**. The highest systemic exposures to the chemical were 0.0486 and 0.0466 mg/kg bw/day from use in body lotion and fine fragrances, respectively.

Table 1 – Daily systemic exposure to cosmetic products (dermal exposure)

Product type	Amount (mg/day)	C (%)	RF (unitless)	Daily systemic exposure (mg/kg bw/day)
Body lotion	7820	0.3	1	0.0486
Fine fragrances	750	3.0	1	0.0466
Hand cream	2160	0.3	1	0.0134
Face cream	1540	0.3	1	0.0096
Deodorant (non-spray)	1500	0.3	1	0.0093
Nail polish	50*	5.0	1	0.0052
Liquid foundation	510	0.3	1	0.0032
Hair styling products	4000	0.3	0.1	0.0025
Shower gel	18,670	0.3	0.01	0.0012
Shampoo	10,460	0.3	0.01	0.0006
Conditioner	3920	0.3	0.01	0.0002

Daily systemic exposure = (Amount × C × RF × DA)/BW with DA = 12.42% and BW = 60 kg
C = chemical concentration; RF = retention factor; DA = dermal absorption; BW = body weight
*refers to amount of nail product directly in contact with skin as absorption through the nail plate is negligible as per the RIVM cosmetics fact sheet (RIVM 2006).

The limited specific information on these uses in personal care products indicates that current uses in these products may not be widespread. This may be due to the chemical being prohibited in consumer products in the EU and the proposed increasing of restrictions in Canada. Therefore, it is unlikely that an individual has daily exposure to multiple personal care products containing the chemical.

The chemical has identified uses in domestic products that are expected to be used frequently in the home including scented candles and cleaning spray products. The ConsExpo web tool v 1.2.0 was used to estimate the worst case daily systemic exposure to the chemical (RIVM n.d.).

The following default values and assumptions were used in all estimates (Enhealth 2012; RIVM 2018; RIVM 2021):

- Dermal exposure model – Direct Product Contact.
- Absorption model – Fixed fraction.
- Default adult inhalation rate – 20 m^3/day (except for candles).
- Mass transfer coefficient – 10 m/hr.

The concentration was assumed to be 0.3% in both products based on information from Health Canada (see **Introduction and use**). Estimates were calculated using standard assumptions and estimates provided by the relevant RIVM product fact sheets as referenced in **Table 2**.

In the cleaning spray scenario, the dermal exposure is a sum of contributions from the incidental dermal contact with sprays and dermal contact with a cloth during rinsing.

For scented candles, only inhalation exposures were considered. A default inhalation rate of 0.55 m^3/hr (resting) was used (RIVM 2021).

The estimates are presented in **Table 2**. The total daily systemic exposure to the chemical was 0.004 and 0.031 mg/kg bw/day for cleaning sprays and candles, respectively.

Table 2 – Daily systemic exposures to frequently used domestic products

Product type (concentration)	RIVM scenario	Dermal ConsExpo model settings	Dermal exposure (mg/kg bw/day)	Inhalation ConsExpo model	Inhalation exposure (mg/kg bw/day)	Total exposure (mg/kg bw/day)
Cleaning spray (0.3%)	All-purpose cleaning spray (RIVM 2018)	Constant rate (spraying) Instant application (rinsing)	0.002	Exposure to spray - spraying	0.002	0.004
Candles (0.3%)	Scented candles (RIVM 2021)	-	-	Exposure to vapour - constant rate	0.031	0.031

Acute exposures – less frequently used products

The chemical also had identified uses in consumer products that are expected to be used less frequently than the above personal care and domestic products. These products included paints and stains (see **Introduction and use**). For these products, the worst case systemic exposure estimates were considered on a per event basis rather than by daily exposure. Limited exposure is expected from use of benzophenone in inks as they are expected to be contained in sealed cartridges.

The ConsExpo web tool v 1.2.0 was used to estimate the dermal and inhalation systemic exposures to the chemical when used in these less frequently used products (RIVM n.d.). These estimates typically represent the worst case scenario exposures to these products. The following default values and assumptions were used in all estimates (Enhealth 2012; RIVM 2018; RIVM 2021):

- Dermal exposure model – Direct Product Contact.
- Absorption model – Fixed fraction.
- Default adult inhalation rate – 20 m^3/day.
- Mass transfer coefficient – 10 m/hr.

Estimates were calculated using the standard assumptions and estimates provided by the relevant RIVM product fact sheets as referenced in **Table 3**.

For paints and stains, the concentrations were 0.3% and based on information available from the CPID (see **Introduction and use**). The dermal exposure estimate for interior wall paints and exterior wood stains are based on the same scenario and; therefore, have the same value. However, exterior wood stains are expected to be used outdoors where inhalation exposure is expected to be negligible with high ventilation.

The estimates of systemic exposure to the chemical are summarised in **Table 3**. The total systemic exposures to the chemical from these products were in the range 0.022–0.023 mg/kg bw per event.

Table 3 – Acute exposures to benzophenone from domestic products calculated using ConsExpo web tool

Product type (concentration)	RIVM scenario	Dermal ConsExpo model settings	Dermal exposure (mg/kg bw/event)	Inhalation ConsExpo model	Inhalation exposure (mg/kg bw/event)	Total exposure (mg/kg bw/event)
Interior wall paint (0.3%)	Brush/roller painting, waterborne wall paint (RIVM 2007)	Constant rate	0.022	Exposure to vapour - evaporation from increasing area	0.0006	0.023
Exterior wood stain (0.3%)	Brush/roller painting, waterborne wall paint (RIVM 2007)	Constant rate	0.022	-	-	0.022

Exposures from other sources

Benzophenone is both an impurity and degradation product in personal care products that contain octocrylene (AICIS 2025). The amount of the chemical in products containing octocrylene was measured in a study and expressed as an amount of benzophenone per weight of product (Downs et al. 2021). The maximum amount of benzophenone detected was 461.4 mg/kg product, measured in a sunscreen sample that was subjected to a 6 week US FDA accelerated stability testing protocol. Using the personal care products identified in the AICIS evaluation of octocrylene and the maximum benzophenone concentration detected in the sunscreen study, the worst case systemic exposure to benzophenone as an impurity/degradation product in octocrylene-containing products was estimated and shown in **Table 4**. The aggregate daily systemic exposure to the chemical from these products was 0.0134 mg/kg bw/day.

Table 4 – Estimated daily systemic exposure to benzophenone from cosmetic products containing octocrylene

Product type	Product amount (mg/day)	Amount benzophenone (mg/day)	Daily systemic exposure (mg/kg bw/day)
Lipstick, lip balm	57	0.03	0.0004*
Body lotion	7820	3.61	0.0075
Face cream	1540	0.71	0.0015
Fine fragrance	750	0.35	0.0007
Hand cream	2160	1.00	0.0021
Liquid foundation	800	0.37	0.0008

Product type	Product amount (mg/day)	Amount benzophenone (mg/day)	Daily systemic exposure (mg/kg bw/day)
Nail varnish remover	500	0.23	0.0005
Total	-	**6.29**	**0.0134**

Daily systemic exposure = (Benzophenone amount × DA)/BW with DA = 12.42% and BW = 60 kg
DA = dermal absorption; BW = body weight
*oral exposure considered with an oral absorption value of 100% assumed

In the octocrylene study, the average baseline concentration of the chemical before the 6-week accelerated aging study was 39 mg/kg product (Downs et al. 2021). This is approximately 12 times lower than the maximum value used in this exposure estimate. The daily systemic exposure to the chemical from products that have not aged significantly would; therefore, be approximately an order of magnitude lower than the estimate.

The chemical is both a natural flavour and used as a food additive. For a 60 kg adult, EFSA estimated that the combined chronic dietary exposure to the chemical is 0.0085 mg/kg bw/day. EFSA also noted that benzophenone may migrate from food contact materials with a worst case estimated exposure of approximately 0.01 mg/kg bw/day (EFSA 2017). FSANZ undertook a screening survey of packaging chemicals as part of the 24th Australian Total Diet Study. This screening assessment conducted by FSANZ found that estimated exposures to benzophenone were below the TDI established by EFSA and that the public health and safety risk from benzophenone is low.

Health hazard information

This evaluation of benzophenone reviews available data relating to carcinogenicity.

In addition, details of toxicological data that have been used for quantitative risk assessment (see **Public risk** section) have been summarised. This summary includes information on toxicokinetics, repeat dose toxicity and maternal toxicity effects in a developmental toxicity study.

More information on other endpoints not considered in this evaluation are available in the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework report conducted under the former scheme, the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (NICNAS 2015).

Toxicokinetics

Absorption

The chemical can be absorbed following oral and dermal exposure. There are no data on absorption from inhalation.

Following oral administration, the chemical was rapidly absorbed from the gastrointestinal tract in rats (NICNAS 2015).

A dermal absorption value of 12.42% (max value + 1 standard deviation) was determined for therapeutic sunscreen products. In the GLP compliant guideline study (Organisation for

Economic Co-operation and Development (OECD) Test Guideline (TG) 428), [^{14}C]-benzophenone was added (0.6 g/L benzophenone) to 2 commercial sunscreen formulations and neat acetone then applied (approximately 2 µL/cm^2) to dermatomed human skin mounted in static diffusion cells. After 24 hours, the amount of benzophenone absorbed from the 2 spiked sunscreen formulations was 9.04 ± 2.61% and 10.02 ± 2.40%. The study did not consider the potential for benzophenone metabolism by skin enzymes because the skin was frozen until it was used in the test. These results are conservative because ethanol and acetone can increase the solubility of benzophenone in the formulation and lead to greater dermal absorption compared with formulations that do not contain these solvents. Human skin is preferred for dermal absorption studies or pig skin if human skin is not available (Ejaz et al. 2024).

Dermal absorption in monkey studies was much greater (in line with previous). The percutaneous absorption (occluded) of [^{14}C] benzophenone in rhesus monkeys was approximately 70% within 24 hours. Dermal absorption was reduced to 44% under unoccluded conditions, presumably because the chemical evaporated (NICNAS 2015; Ejaz et al. 2024).

Metabolism

In rabbits, the main metabolite is benzhydrol (CAS No. 91-01-0). In isolated Fischer 344 (F344) rat hepatocytes, 3 metabolites of the chemical were identified: benzhydrol, and 4-hydroxybenzophenone (CAS No. 1137-42-4) and its sulfate conjugate. The main metabolites in *in vivo* and *in vitro* studies in rats are benzhydrol and 4-hydroxybenzophenone and their sulfate and glucuronide conjugates (Government of Canada 2021; NICNAS 2015).

Following exposure of an aqueous solution of the chemical to UV or sunlight irradiation, 3-hydroxybenzophenone, 4-hydroxybenzophenone were observed, together with concomitant production of hydrogen peroxide. This suggests 'that benzophenone might act as a photosensitiser' to generate reactive oxygen species 'which can cause aromatic ring hydroxylation' (NICNAS 2015).

Distribution

The main metabolites of benzophenone are likely to circulate as the sulfate and glucuronide conjugates to the small intestine through the biliary system and back into the liver (NICNAS 2015; EFSA 2009).

Excretion

Mice excrete benzophenone more rapidly than rats. The elimination half-life of the chemical (parent compound) is approximately 19 hours (gavage) in SD rats, 4 hours (intravenous (i.v.) injection) and 8 hours (gavage) in F344 rats, and approximately one hour (i.v. injection) and 1.5 hours (gavage) in mice (Government of Canada 2021; NICNAS 2015).

Benzhydrol glucuronide is the primary form excreted through urine in rats (NICNAS 2015). A small amount (1%) of the administered dose (100 mg/kg bw) was detected as 4-hydroxybenzophenone in enzyme-treated urine samples. None was detected in the faeces.

In human studies benzophenone derivatives were detected in all urine samples from 14 healthy volunteers. Benzhydrol was measured as 0.27–10.0 ng/mL. No benzophenone was found in any of the samples (IARC 2013).

Repeat dose toxicity

Oral

Based on the available data, the chemical is not considered to cause severe effects following repeated oral exposure. The severity of the adverse effects or doses at which effects were observed in various organs is not sufficient to warrant hazard classification.

Three subchronic (1–3 months) dietary animal studies showed that the liver and kidneys were the primary target organs for the toxicity of the chemical. Effects included:

- increased organ weights and microscopic changes in the liver and kidneys
- clinical chemistry changes
- increased induction of liver enzymes.

Effects were observed at all doses in 2 of the studies (doses ≥ 75 mg/kg bw/day in a rat study and ≥ 200 mg/kg bw/day in a mouse study). In the third study in rats (described in more detail below) an NOAEL of 20 mg/kg bw/day was established (NICNAS 2015).

In a repeated dose oral study, Sprague Dawley (SD) rats were administered (in diet) the chemical at 20 mg/kg bw/day for 90 days (32/sex), or 100 or 500 mg/kg bw/day (12/sex or 10/sex respectively) for 28 days. The initial dosing was staggered over a 7 day period because this study was part of a larger investigation involving 3 other test substances. As a consequence, meaningful statistical evaluation of body weights, food consumption and organ weights of the mid- and high- dose groups could not be undertaken. After 4 weeks of treatment, increased mean absolute and relative liver and kidney weights were observed at ≥ 100 mg/kg bw/day. Histopathological examination of the liver in the mid- and high-dose groups revealed hepatocellular enlargement with associated clumping of cytoplasmic basophilic material around the central vein. Treatment related effects observed at the mid- and high-dose levels were significant changes in erythrocyte counts, haemoglobin, haematocrit, total protein and albumin concentrations at ≥ 100 mg/kg bw/day. The NOAEL was established as 20 mg/kg bw/day for 90 days (NICNAS 2015; Burdock et al. 1991).

The effects on the liver and kidneys seen in repeated dose toxicity studies were also reported in reproductive toxicity and carcinogenicity studies. These effects were:

- liver hypertrophy in a 2-generation rat study (~6 mg/kg bw/day) (EFSA 2017) and in carcinogenicity studies in rats and mice (in all treated groups from 15 mg/kg bw/d in rats and 35 g/kg bw/d in mice)
- nephropathy and mineralisation in the kidneys of all treated rats (from 15 mg/kg bw/d) and renal tubule hyperplasia in all treated rats and severe nephropathy in male rats reported in 2 year carcinogenicity studies (ECHA 2020).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

The chemical was not considered to be genotoxic based on *in vitro* and *in vivo* guideline studies (EFSA 2017; IMAP 2015; ECHA 2020). The metabolite of the chemical 4-hydroxy benzophenone (CAS No. 1137-42-4) was also considered non-genotoxic in *in vitro* and *in vivo* tests (REACH n.d.-b).

Carcinogenicity

The chemical is classified as 'Carcinogenicity — Category 2 (H351): 'Suspected of causing cancer' in the HCIS (SWA n.d.). Consideration of the following evidence supports amending this classification to the hazard category 'Carcinogenicity — Category 1B' and the hazard statement 'H350 — May cause cancer'. In animals, the chemical caused:

- benign and malignant tumours in several organ systems including increased incidences of the rare tumours histocytic sarcoma (in female rats and mice) and hepatoblastoma (in male mice)
- other neoplastic and non-neoplastic effects in the liver, kidneys, and haematopoietic system including the spleen.

As there is no established mechanism to determine the carcinogenicity of the chemical, the relevance to humans cannot be ruled out. The chemical is considered to be a threshold carcinogen as it is non-genotoxic.

Animal data

In a 2-year carcinogenicity study (OECD TG 451), groups of B6C3F1 mice (50/sex/dose) were administered the chemical (purity > 99%) in the diet at concentrations of 0, 312, 625 or 1250 ppm (males: 0, 40, 80 or 160 mg/kg bw/day; females: 0, 35, 70 or 150 mg/kg bw/day). The following findings were reported (see **Tables 5** and **6** below) (ECHA 2020, NTP 2006):

- The incidence of histiocytic sarcoma in females was significantly increased in the mid-dose group (625 ppm) and exceeded the historical control data (HCD) (mean of 0.3%; range 0–2%) in the mid- and high-dose groups. Multiple organs throughout the bodies of females with histiocytic sarcomas in the high-dose group had neoplastic lesions.
- An increased incidence of hepatoblastomas in male mice was reported as 0, 1 (2%), 1 (2%) and 3 (6%) in control, low-, mid- and high-dose groups respectively. The findings were not statistically significant but they did exceed the HCD incidence (range 0–2%, mean 0.2%).
- In males, a positive trend in the incidence of combined hepatocellular neoplasms (primarily adenomas) were observed in all treatment groups, and incidences at the highest dose were significantly greater than the controls (18 (36%), 20 (40%), 25 (50%) and 29 (58%) for controls, low-, mid- and high-dose respectively) (NTP 2006). The incidence of hepatocellular adenomas in males showed a clear dose-response relationship. The increases were statistically significant in the mid- and high-dose groups which exceeded the HCD. In females, the increased incidence of hepatocellular adenoma was observed in the mid- and high-dose groups. The incidence was reported to be more than expected when corrected for decreased body weight (NTP 2006, ECHA 2020).
- Hepatocellular carcinomas were observed in treated males at non-significant incidences and only single incidences were reported in treated females in the low- and high-dose groups.

- Other observations in both sexes include significantly increased incidence of metaplasia of the olfactory epithelium (1250 ppm) and significantly increased hyperplasia of lymphoid follicles in the spleen of all treated males, and in females in the low- and mid-dose groups.
- A statistically significant increase in the incidence of hypertrophy of hepatocytes in all treated groups in both sexes. Active chronic inflammation was observed in the liver of males but not females (ECHA 2020; NICNAS 2015; NTP 2006).

An NOAEL could not be determined because there were effects in all treated groups.

Table 5 Incidences of neoplastic lesions in male mice

Tumour type	0 ppm (0 mg/kg bw/d)	312 ppm (40 mg/kg bw/d)	625 ppm (80 mg/kg bw/d)	1250 ppm (160 mg/kg bw/d)	Historical control
Hepatocellular adenoma	11 (22%)	15 (30%)	23* (46%)	23* (46%)	(feed) 9/460, range 12–30%, mean 20%
Hepatocellular carcinoma	8 (16%)	5 (10%)	6 (12%)	6 (12%)	(all routes) 8–46%, mean 22.9%, 1257 controls
Hepatoblastoma	0 (0%)	1 (2%)	1 (2%)	3 (6%)	(feed); 1/460, range 0–2%, mean 0.2%
Hepatocellular adenoma, carcinoma or hepatoblastoma	18 (36%)	20 (40%)	25 (50%)	29* (58%)	145/460, range 20–47%, mean 32%

* Statistically significantly different (P ≤ 0.05) from the control group.

Table 6 Incidences of neoplastic lesions in female mice

Tumour type	0 ppm (0 mg/kg bw/d)	312 ppm (35 mg/kg bw/d)	625 ppm (70 mg/kg bw/d)	1250 ppm (150 mg/kg bw/d)	Historical control
Hepatocellular adenoma	5 (10%)	4 (8%)	10 (20%)	8* (16%)	40/457, range 6–12%, mean 9.6%
Hepatocellular carcinoma	0 (0%)	1 (2%)	0 (0%)	1 (2%)	-
Hepatoblastoma	Not reported	Not reported	Not reported	Not reported	-
Hepatocellular adenoma or carcinoma	5 (10%)	5 (10%)	10 (20%)	9* (18%)	53/457, range 8–16%, mean 11.8%
Histiocytic sarcoma	0 (0%)	0 (0%)	5* (10%)	3 (6%)	2/459, range 0–2%, mean 0.3%

*Statistically significantly different (P ≤ 0.05) from the control group.

In a 2-year carcinogenicity study (OECD TG 451), F344/N rats (50/sex/dose) were fed diets containing the chemical at doses of 0, 312, 625 or 1250 ppm (males: 0, 15, 30 or 60 mg/kg bw/day; females: 0, 15, 30 or 65 mg/kg bw/day) (NTP 2006). The following effects were reported (see **Table 7** and **8** below) (ECHA 2020; NTP 2006):

- Rare histiocytic sarcomas were observed in 3 female rats (one in the mid-dose group and two in the high-dose group).
- In males, there was a positive trend in the incidence of renal tubule adenoma (reaching statistical significance at the highest dose) accompanied by increased incidence of renal tubule hyperplasia and increased pelvic transitional epithelium hyperplasia (all exposed groups) (NTP 2006).
- Mononuclear cell leukaemia (MCL) was reported in all rats including controls (statistically significant at low- and mid-doses for males and mid-doses for females).
- Non-neoplastic liver effects included significantly increased incidences of centrilobular hepatocellular hypertrophy (all exposed groups), cystic degeneration of hepatocytes (mid- and high-dose males), and bile duct hyperplasia (statistically significant increases in all exposed females) (NICNAS 2015; NTP 2006). The lowest observed adverse effect level (LOAEL) was determined to be 15 mg/kg bw/d based on the renal tubule hyperplasia (all treated rats), bile duct hyperplasia (all treated females) and severity of nephropathy (all treated males). An NOAEL could not be determined because there were effects in all treated groups.

Table 7 Incidence of neoplastic lesions in male rats

Tumour type	0 ppm (0 mg/kg bw/d)	312 ppm (15 mg/kg bw/d)	625 ppm (30 mg/kg bw/d)	1250 ppm (60 mg/kg bw/d)	Historical control
					(feed)
Mononuclear cell leukaemia	27 (54%)	41* (82%)	39* (78%)	24 (48%)	231/460 range 30–68% (mean 49.1%)
Histiocytic sarcoma	Not reported	Not reported	Not reported	Not reported	-
Renal tubule adenoma	2 (4%)	2 (4%)	7 (14%)	8* (16%)	0–2% in 1152 controls

*Statistically significantly different (P ≤ 0.05) from the control group.

Table 8 Incidences of neoplastic lesions in female rats

Tumour type	0 ppm (0 mg/kg bw/d)	312 ppm (15 mg/kg bw/d)	625 ppm (30 mg/kg bw/d)	1250 ppm (65 mg/kg bw/d)	Historical control
					(feed)
Mononuclear cell leukaemia	19 (38%)	25 (50%)	30* (60%)	29 (58%)	112/460 range 12–38% (mean 24.6%)
Histiocytic sarcoma	0 (0%)	0 (0%)	1 (2%)	2 (4%)	(feed): 0/460. All routes range 0–2%, mean 0.1%, 1/1209.
Renal tubule adenoma	Not reported	Not reported	Not reported	Not reported	-

*Statistically significantly different (P ≤ 0.05) from the control group.

Negative results were reported for benzophenone in dermal carcinogenicity studies with concentrations up to 50% applied to the skin of Swiss mice and New Zealand White (NZW) rabbits, up to 160 weeks of treatment (NICNAS 2015).

After evaluating the available data in animals, IARC classified the chemical as '*possibly carcinogenic to humans (Group 2B)*'. IARC concluded that 'There is *sufficient evidence* in experimental animals for the carcinogenicity of benzophenone' (IARC 2013).

Regarding the weight of evidence supporting amending the GHS classification to Cat 1B, AICIS notes the following:

- **Histiocytic sarcomas** (white blood cell cancer) – A positive trend in the increased incidence was observed in female rats and mice. The tumour was more invasive in female mice in the high dose group. The findings were supported by increased haematopoietic cell proliferation in the spleen of all treated female mice. Although the increased incidence was only statistically significant in mice, the incidence was above historical controls in the mid- and high-dose females in both rats and mice. The incidence of this tumour was low as expected for a tumour that is considered to be extremely rare in rats and mice. The results are considered to be treatment related and biologically significant (ECHA 2020; EFSA 2017).
- **Hepatoblastomas** (liver cancer) – Although the increased incidence in male mice was small (not statistically significant), it showed a positive trend in relation to treatment. It is a rare tumour type and exceeded historical controls. Hepatoblastomas are malignant neoplasms that are presumed to be a primitive form of hepatocellular carcinoma (ECHA 2020; NTP 2006).
- **Hepatocellular adenomas** (benign liver tumours) - Dose-response relationships were observed in male mice and incidences in female mice were greater than HCD.
- The positive trend in incidences of **combined hepatocellular adenoma, carcinoma or hepatoblastomas** in male mice. The National Toxicology Program (NTP) considered this to be "some evidence of carcinogenicity" (NTP 2006).
- There is uncertainty regarding the human relevance of chronic kidney effects such as chronic progressive nephropathy in rats (ECHA 2020). Nevertheless, the induction of **renal tubule adenomas** adds to the weight of evidence of carcinogenicity because proliferative lesions and adenomas may be considered as a biological and morphological continuum in the development of kidney tumours (EFSA 2017).
- A positive trend in the incidence of renal tubule adenomas was found in the treated male rats with statistical significance reported at the high dose and statistically significant increases in **renal tubule hyperplasia** observed in all treated rats.
- The European Chemicals Agency (ECHA) found that the observations for histiocytic sarcomas and hepatoblastomas supported amending the GHS classification of benzophenone to category 1B given that they provided evidence of carcinogenicity in different tissues in two animal species at doses which were not excessive (ECHA 2020).

Reproductive and development toxicity

Based on the available data, the chemical is not considered to have specific reproductive or developmental toxicity. Some developmental effects were observed in a 2-generation reproductive and developmental study in rats and 2 developmental toxicity studies in rats and rabbits secondary to maternal toxicity (NICNAS 2015).

Maternal toxicity effects were identified as the basis for the point of departure used for the quantitative risk assessment for acute exposures (see **Human health risk characterisation**). Maternal toxicity including reduced maternal bodyweight was reported in a number of toxicological studies. The lowest NOAEL was observed in a rabbit study summarised below.

In an NTP developmental toxicity study, NZW rabbits (n = 24/dose) were administered the chemical (gavage) at doses of 0, 5, 25 or 45 mg/kg bw/day from gestational days (GD) 6–29. Maternal toxicity was observed at 25 mg/kg bw/day, which included reduced body weight and food consumption, dose related maternal mortality and early termination of pregnancy (abortion or early delivery). No changes were observed for the gravid uterus, liver or kidney weights. Developmental toxicity effects included significantly reduced average foetal weight per litter at the highest dose. No adverse effects on prenatal viability or incidences of foetal morphological anomalies among litters were observed. The authors stated that 'developmental toxicity was noted only in the presence of well-defined maternal toxicity', which is a similar finding to the rat studies (NTP 2006). The maternal and developmental NOAELs were determined to be 5 mg/kg bw/day and 25 mg/kg bw/day, respectively (NICNAS 2015; NTP 2004).

Endocrine effects

There is evidence that the chemical interacts with the endocrine system but there is limited evidence of adverse effects.

The chemical was found to interact with the oestrogen and thyroid receptors in *in vitro* assays. In uterotrophic assays, an increased uterine weight was observed following oral and intraperitoneal administration but only at doses > 300 mg/kg bw/day. No effects were observed following subcutaneous injection. The metabolite 4-hydroxybenzophenone has been shown to elicit an oestrogenic effect in several uterotrophic assays.

There is no evidence of endocrine disrupting properties in long term studies including a 2-generation reproductive toxicity study.

The European Food Safety Authority (EFSA) concluded that the outcomes from reproductive and developmental toxicity studies on benzophenone found no clear evidence of endocrine disruption. These studies included results from extra endpoints specifically targeting the endocrine system. They acknowledged positive results in uterotrophic assays in rats but considered it to be of uncertain relevance for risk assessment because effects were observed at high doses only. EFSA also concluded that the endocrine activity reported for benzophenone and its metabolite 4-hydroxybenzophenone is weak and; therefore, a threshold mode of action can be assumed (EFSA 2017).

Benzophenone is listed in the EC Endocrine Disruptors Priority List under Category 3b classification (i.e. no evidence of endocrine disrupting activity or no data available); and the US EPA's Universe of Chemicals list for potential endocrine disruptor screening and testing (NICNAS 2015).

ECHA published a Decision on Substance Evaluation for benzophenone (ECHA 2018) in which oestrogenic, anti-androgenic and thyroidal activities of the substance were discussed. ECHA noted that the submitted long term studies on benzophenone did not provide evidence for endocrine disruption due to oestrogenic properties. However, ECHA acknowledged that some parameters were not investigated. The report concluded that the overall weight of evidence indicates that benzophenone is not likely to disrupt thyroid function in rodents *in vivo* based on a large number of long term rodent studies. Although uncertainties remain regarding the oestrogenic mode of action, ECHA did not recommend prioritising this chemical for further investigations for the endocrine mode of action. This was determined due to the:

- additional risk management measures from benzophenone's carcinogenicity classification would lead to a reduced risk including from any potential effect on the endocrine system
- difficulties associated with pursuing appropriate investigations.

Human health risk characterisation

Public risk

Chronic exposures – frequently used products

For chronic exposures, the point of departure is best represented by TDI of 0.03 mg/kg bw/day set by EFSA (EFSA 2017). The TDI was derived based on non-neoplastic kidney effects observed in a chronic toxicity study. EFSA considered this TDI sufficiently protective for the non-neoplastic effects in repeat dose toxicity studies and the neoplastic effects in the carcinogenicity studies.

For most personal care products, the estimate of systemic exposure to the chemical was less than 50% of the TDI, indicating a low health risk to the public from the individual use of these products. However the exposure estimates for two use scenarios exceeded the TDI. These were the use of the chemical in body lotion at concentrations of 0.3% and fine fragrances at concentrations of 3.0% which were 162% and 155%, respectively (see **Table 8**). Reduced concentrations of 0.1% and 1% for body lotion and fine fragrance respectively would result in exposures that are approximately 50% of the TDI.

Table 9 – Contribution of worst-case daily dermal systemic exposure to benzophenone from cosmetic products as a percentage of the TDI

Product type	Daily systemic exposure (mg/kg bw/day)	Percentage of tolerable daily intake
Body lotion	0.0486	162%
Fine fragrances	0.0466	155%
Hand cream	0.0134	45%
Face cream	0.0096	32%
Deodorant (non-spray)	0.0093	31%
Nail polish	0.0052	17%
Liquid foundation	0.0032	11%
Hair styling products	0.0025	8.3%
Shower gel	0.0012	3.9%
Shampoo	0.0006	2.2%
Conditioner	0.0002	0.8%

The aggregate exposure to the chemical from use of all personal care products also exceeds the TDI. However, the limited specific information on these uses in personal care products indicates that current uses in these products may not be widespread. This may be due to the prohibition in consumer products in the EU and the proposed increase of restrictions in Canada. Therefore, it is unlikely that an individual has daily exposure to multiple personal care products containing the chemical.

For cleaning products, the worst case systemic exposure estimate was 0.004 mg/kg bw/day (see **Human exposure**). This value is 13% of the TDI.

For scented candles, the worst case systemic exposure estimate was 0.031 mg/kg bw/day (see **Human exposure**). This value is approximately the same as the TDI. The estimate is based on a scenario where a user burns 2 candles for 2 hours approximately 6 times a week on average (RIVM 2021). The estimate for users who only use candles infrequently would be significantly lower than the TDI.

Acute exposures – less frequently used products

A quantitative risk assessment using the margin of exposure (MOE) methodology was used to characterise the risk to human health associated with systemic exposure to the chemical. The margin of exposure (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, an MOE value greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences.

The point of departure for acute exposures to the chemical for public health risk characterisation is maternal toxicity in developmental toxicity studies, for which an NOAEL of 5 mg/kg bw/day was determined (Government of Canada 2021). MOEs were calculated for each of the acute exposures for which exposure to the chemical was estimated (see **Human exposure**) and are presented in **Table 10**. In all scenarios, the MOEs were greater than 100.

Table 10 – Margins of exposure for acute exposures to benzophenone from domestic products

Product type (concentration)	Margin of exposure (dermal)	Margin of exposure (inhalation)	Margin of exposure (total)
Interior wall paint (0.3%)	227	7813	221
Exterior wood stain (0.3%)	227	-	227

Exposures from other sources

Based on the worst case scenario estimates from products containing octocrylene, the aggregate systemic exposure to the chemical as an impurity or degradation product is

0.013 mg/kg bw/day (see **Table 11**). This estimate is approximately 45% of the TDI recommended by EFSA. The daily systemic exposure to the chemical from products that have not aged significantly would be approximately an order of magnitude lower than the estimate.

Table 11 - Contribution of worst case daily systemic exposure to benzophenone as an impurity or degradation from cosmetic products containing octocrylene as a percentage of the TDI

Product type	Daily systemic exposure (mg/kg bw/day)	Percentage of tolerable daily intake
Lipstick, lip balm	0.0004	1.5%
Body lotion	0.0075	25%
Face cream	0.0015	4.9%
Fine fragrance	0.0007	2.4%
Hand cream	0.0021	6.9%
Liquid foundation	0.0008	2.5%
Nail varnish remover	0.0005	1.6%
Total	**0.0134**	**45%**

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