



SCIENTIFIC ADVISORY GROUP ON CHEMICAL SAFETY OF NON-FOOD AND NON-MEDICINAL CONSUMER PRODUCTS (SAG-CS)

Final Opinion on Methyl Salicylate in Cosmetic Products

1. Introduction

1.1 Methyl salicylate (methyl 2-hydroxybenzoate; CAS No. 119-36-8), Figure 1, is not currently listed in the Annexes of the Cosmetic Products Regulation UK No 1223/2009 (as amended)¹. Under the GB Classification, Labelling and Packaging (CLP) regulation No 1272/2008 (as amended)², methyl salicylate has recently been classified as a category 2 reproductive toxicant, as well as in acute toxicity category 4 and skin sensitiser category 1B. Article 15 of the UK Cosmetics Regulation prohibits the use of category 1A, 1B and 2 Carcinogenic, Mutagenic or Reprotoxic (CMR) classified substances in cosmetic products under the GB CLP regulation and which are included in the GB Mandatory Classification and Labelling (MCL) list, unless an exemption has been granted by the Secretary of State³.

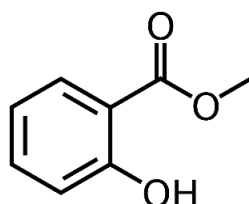


Figure 1: Structure of methyl salicylate (methyl 2-hydroxybenzoate)

¹ The UK Regulation currently consists of the Regulation UK No 1223/2009 as amended by [SI 696/2019 Product Safety and Metrology \(EU Exit\) Regulations](#). The full consolidated UK text will be available soon.

² The GB CLP Regulation No 1272/2008 as amended by The Chemicals (Health and Safety) and Genetically Modified Organisms (Contained Use) (Amendment etc.) (EU Exit) Regulations 2019. The full consolidated UK text will be available soon.

³ Guidance on the management of CMR substances under the UK Cosmetics Regulation (2023). Found [here](#)



1.2 In order to obtain an exemption and to ensure the continued use of methyl salicylate in cosmetic products, the UK Cosmetics Industry have provided a dossier of information and original studies to OPSS, aiming to support the safe use of methyl salicylate in the products listed in Table 1.

Table 1) Industry-proposed UK use levels for methyl salicylate in cosmetic products

Type of cosmetic product	Maximum concentration (%)
<i>Hydroalcoholic-based fragrances</i>	0.600
<i>Rinse-off skin & hair products (except hand wash products)</i>	0.060
<i>Hand wash products</i>	0.600
<i>Leave on skin & hair products (non-aerosol)</i>	0.060
<i>Face Make up products</i>	0.050
<i>Lipsticks & lip balm</i>	0.030
<i>Eye make-up products & make-up remover</i>	0.002
<i>Toothpaste</i>	2.520
<i>Mouthwash</i>	0.600
<i>Mouth spray</i>	0.650
<i>Deo spray/aerosol products</i>	0.003
<i>Hair products (spray/aerosol)</i>	0.009
<i>Body Lotion Spray</i>	0.040

1.3 OPSS requests that the SAG-CS assesses the safety of methyl salicylate intended to be used within cosmetic products.

2. Background

Intended function and uses of methyl salicylate.

2.1 Methyl salicylate is found naturally, as the main component (up to 99%) of wintergreen oil which is extracted predominantly from wintergreen leaves (*Gaultheria procumbens*), or sweet birch bark (*Betula lenta*). Methyl salicylate can also be produced synthetically by the esterification of salicylic acid (Clark IV, 1999).

2.2 Methyl salicylate is used in a variety of cosmetic products, functioning as a flavouring or soothing agent in oral hygiene products, or as a fragrance ingredient. Methyl salicylate may be found in hair products, bathing products, perfumery, make-up, and oral hygiene products, amongst others (Lapczynski et al., 2007).



2.3 Methyl salicylate is found in other consumer products including household cleaners and detergents, air fresheners, biocides (e.g., disinfectants), polishes and waxes. Methyl salicylate is also found in surgical spirit BP and in many over the counter medical topical creams which provide relief from muscle/joint pain. In these creams, methyl salicylate is often present at high concentrations (4.9-40%) and up to 99% in pure oil of wintergreen (Muniandy and Sinnathamby, 2012; [SCCS, 2021](#)). Finally, methyl salicylate can be present in foods (Clarke IV, 1999), including as a flavouring ingredient (Greene et al., 2017), and is permitted for use in GB as stated in the register of flavourings⁴.

2.4 In 2002, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) concluded that intakes of methyl salicylate when consumed as a flavouring agent in food in Europe and the USA would be within the Acceptable Daily Intake (ADI) of 0.5 mg/kg bw/day (JECFA, 2002).

2.5 Methyl salicylate is metabolised in the body to salicylic acid, methanol, and salicylate conjugates. Salicylic acid is also found in cosmetic products and is classified as a category 2 reproductive toxicant under GB CLP Regulation No. 1272/2008 (as amended)⁵. The safety of salicylic acid has previously been assessed by the SAG-CS in [2021](#).

3. Previous Scientific Opinions on Methyl Salicylate

3.1 The safety of methyl salicylate has been evaluated by the Scientific Committee on Consumer Safety (SCCS), initially in 2021 and again in 2023, following revised concentrations submitted by industry to support safe use for children ([SCCS, 2021](#) and [SCCS, 2023a](#)). The Committee for Risk Assessment (RAC) have also published an opinion on the proposed harmonised classification and labelling, at EU level, of methyl salicylate ([RAC, 2019](#)).

3.2 The RAC opinion, published in 2019, recommended a classification of methyl salicylate as 'Toxic for Reproduction Category 2' (suspected of damaging the unborn child) and 'Skin sensitizer Category 1B', based on read across with salicylic acid ([RAC, 2019](#)). Consequently, in 2022, methyl salicylate was added to Annex IV of Regulation (EC) 1272/2008 on

⁴ Flavouring authorisations- Food Standards Agency <https://data.food.gov.uk/regulated-products/flavouring-authorisations?search=methyl+salicylate>

⁵ The GB CLP Regulation No 1272/2008 as amended by The Chemicals (Health and Safety) and Genetically Modified Organisms (Contained Use) (Amendment etc.) (EU Exit) Regulations 2019. The full consolidated UK text will be available soon.



classification, labelling, and packaging of chemical substances and mixtures (CLP regulation) as a CMR category 2 substance.

3.3 In 2021, the SCCS published their finalised opinion on methyl salicylate which took into consideration safety data on methyl salicylate and the RAC opinion on methyl salicylate ([RAC, 2019](#)). It should be noted that following the publication of a preliminary opinion on methyl salicylate in 2021, the SCCS concluded that 'Methyl salicylate is safe when used in cosmetic products up to the maximum concentrations provided in the dossier submitted by the applicant, except for mouth washes used below 10 years old. Following this conclusion, the applicant submitted a revised concentration of 0.1% methyl salicylate for mouthwashes used by children aged 10 years and below. The final SCCS (2021) opinion takes into account this revised concentration and not the original proposed value of 0.6%.

3.4 In their safety assessment, the SCCS (2021) used a NOAEL of 75 mg/kg bw/day as derived from the 3-generation rat feeding study, conducted by Collins et al., (1971). The SCCS also agreed with the applicant that 100% oral absorption should be considered based on evidence of 'rapid and almost complete absorption' of methyl salicylate via the oral route, and that for dermally applied products, a dermal absorption value of 50% should be applied as a default after considering the highly variable nature of values reported across absorption studies. A dermal absorption of 100% is used for lip products. In their exposure assessment, the SCCS decided to include mouth sprays in the aggregate scenario given that it is realistic to consider that toothpaste, mouthwash, and mouth spray may all be used on the same day by adults. For inhalation exposure, the SCCS considered a respiration rate of 0.013m³/min as used in Rothe et al., (2011), rather than the value of 0.009m³/min used by the applicant. This increased the systemic exposure doses calculated for inhalation (SED_{inhalation}) by a factor of 1.44, however, exposure to methyl salicylate by inhalation was still low. The SCCS used a small study by Ficheux and Roudout, (2017) to obtain product use amount data for children's exposure to dermally applied cosmetic products. This study assessed product use amounts in French girls aged 4-14 years.

3.5 Overall, the SCCS concluded that methyl salicylate is safe when used in cosmetic products up to the maximum concentrations provided in the dossier submitted by the applicant. These concentrations are the same as in Table 1 in this paper, with the exception of mouthwash where the following concentrations were assessed: 0.1% (children under 10 years) and 0.6% (ages 10 years and above).



Considering the RAC (2019) opinion, the SCCS concluded that methyl salicylate should be considered as a weak skin sensitiser and an eye irritant in humans. Finally, the SCCS raised some concerns over the additional exposure to methyl salicylate from other products, which has the potential to increase the systemic exposure dose and exceed the safe level. Because of the rapid metabolism of methyl salicylate to salicylic acid, concerns were also raised over the combined exposure to cosmetic products containing various salicylates which may further increase the systemic exposure dose.

3.6 In May 2023, the SCCS published a preliminary opinion on the safety of methyl salicylate for children following additional safety data submitted by industry for children and their final opinion was published in September 2023 ([SCCS, 2023a](#)). The concentrations of methyl salicylate submitted were:

Infants and Toddlers aged 0-3 years- a maximum concentration of 0.02% for all cosmetic products intended for children, excluding toothpaste which has a maximum concentration of 2.52%.

Children aged 3-6 years- the current maximum concentrations as in Table 1. Products not intended for or habitually used by children are excluded (mouthwash, hydroalcoholic-based fragrances, make-up and deodorant).

As in the 2021 SCCS opinion, a NOAEL of 75mg/kg bw/day was used as the Point of Departure, as derived from Collins et al., (1971). An oral bioavailability of 100% is assumed and a default dermal absorption value of 50% used for all products except for lip products where 100% is used. The amount of cosmetic product dermally applied on children for each age category (0.5-1 years (Infants), 1-3 years (Toddlers), and 3-6 years (Children)) and product type was estimated using body surface area and body weight data from EFSA (2012a) based on Sharkey et al., (2001). The SCCS concluded that the use of methyl salicylate is safe in cosmetic products intended for children aged 0.5-3 years when used up to a maximum concentration of 0.02% in shower gel, hand soap, shampoo, body lotion, face cream, hand cream and lip products, and up to 2.52% in toothpaste. For children aged 3-6, the SCCS considers the use of methyl salicylate as safe in cosmetic products intended for this age group (shower gel, hand soap, shampoo, body lotion, face cream, hand cream, lip products and hair conditioner) up to the maximum concentrations presented in Table 1, in addition to a maximum concentration of 2.52% in toothpaste.



Children under 6 months of age were not considered as no data was submitted for this age group.

3.7 The Joint FAO/WHO Expert Committee on Food Additives (JECFA, 2002), United States Environmental Protection Agency (US-EPA, 2005) Biopesticide and Pollution Prevention Division, Norwegian Food Safety Authority (NFSA, 2012) and the European Food Safety Authority (EFSA, 2012b) have all set an acceptable daily intake (ADI) of 0.5mg/kg bw/day for methyl salicylate based on the no observed adverse effect level (NOAEL) of 50 mg/kg bw/day derived from the 2-year oral study in dogs and rodents by Webb and Hansen (1963).

3.8 A number of other published reviews are available including a Cosmetics Ingredient Review (CIR) from 2019. The CIR noted that the Research Institute for Fragrance Materials (RIFM) Expert Panel (Belsito et al., 2007) concluded that “based on the available data, and using a NOAEL value of 50 mg/kg body weight/day as identified in subchronic and chronic toxicity studies, a margin of safety for systemic exposure of humans to the individual salicylates in cosmetic products may be calculated to range from 125 to 2,500,000 (depending upon the assumption of either 12-30% or 100% bioavailability following dermal application) times the maximum daily exposure.” Overall, the CIR concluded that various salicylates, including methyl salicylate, are “safe in cosmetics in the present practices of use and concentration described in the safety assessment, when formulated to be non-irritating and non-sensitizing, which may be based on a quantitative risk assessment (QRA)” (CIR, 2019).

4. Discussion by the Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products (SAG-CS)

4.1 At their July 2023 meeting, the SAG-CS discussed a paper and associated industry-prepared dossier which focused on the available safety data for methyl salicylate when used in cosmetic products at the concentrations listed in Table 1. Safety data were presented for adults and children (infants aged 0.5-1 years, toddlers aged 1-3 years, children aged 3-10 years and adolescents aged 10-18 years).

4.2 Members discussed the dermal absorption of methyl salicylate and agreed on the value of 50% used in the discussion paper and by the applicant. The value of 50% is conservative following consideration of the large



variation of values reported in dermal absorption studies and is the default applied by the SCCS. A dermal absorption of 100% was agreed to be used for lip products, as lips have thin stratum corneum.

- 4.3 Members agreed to use an oral absorption value of 100% based on the evidence of rapid and almost complete absorption of methyl salicylate via the oral route.
- 4.4 Members had concerns surrounding the total exposure to salicylates in general. This includes exposure to methyl salicylate from other sources such as foods and medicinal products as well as exposure to other salicylates for example, from other cosmetic products, household cleaners and medical products. Exposure via food and medicine is outside of the remit of the SAG-CS and is assessed by other departments and committees.
- 4.5 There is limited information in the literature for total salicylate exposure other than a review conducted by the CIR in 2019 (CIR, 2019) which is provided in section 3.8.
- 4.6 Members discussed the metabolism and excretion of methyl salicylate. Methyl salicylate is extensively and rapidly hydrolysed in the body to salicylic acid and methanol. This is the basis for the category 2 CMR classification of methyl salicylate, which followed the category 2 reproductive toxicant classification of salicylic acid.
- 4.7 Methyl salicylate is not considered to be genotoxic, mutagenic, or carcinogenic.
- 4.8 Members agreed that for the children's safety assessment, P5 body weights should be used instead of the mean body weight so as to be appropriately conservative, and protective of the most sensitive populations. The P5 body weight represents the 5th percentile for body weight for the particular age group.
- 4.9 A point was raised concerning the relevance of the point of departure of 75 mg/kg bw/day for children given that this was derived from a 3-generation rodent study, with the LOAEL determined from observations such as decreased litter size (Collins et al., 1971). However, given that NOAELs derived from other studies ranged between 50-100 mg/kg bw/day, and other data is limited, members agreed to continue using this value in the children's safety assessment.



- 4.10 Gas or liquid chromatographic analytical methods for the determination of methyl salicylate in cosmetics and personal care products are available in the literature (Pauwels et al., 2012, and Anyakudo, et al., 2019). Members were thus content that analytical methods could be applied routinely following appropriate validation.
- 4.11 Where acceptable safety margins were not met in the initial safety assessment using the concentrations set out in Table 1, members reviewed additional calculations to identify the maximum use concentrations in which acceptable margins of safety were met. These calculations are presented alongside the initial calculations in Appendix 1 (Safety Assessment) and can be found in Tables 6b, 6c, 7b, 7c, 9c, 10b and 10c. A full list of the tables included in the Safety Assessment can be found on pages 13-15.

5. Conclusions

A summary of the safety assessment can be found in Table 2 (adults), Table 3a (infants) and Table 3b (Toddlers, children, and adolescents).

Use in Adults

Based on the evidence available to the Committee, members agreed that methyl salicylate is acceptable for use by adults at the concentrations as stated in Table 1.

Members also agreed that methyl salicylate is acceptable for use by adults when considering an aggregate of all the product types and exposure routes (dermal, oral and inhalation) as listed in Table 1.

Use in Infants, Toddlers, Children and Adolescents

No specific data was provided for children aged 0-0.5 years; therefore, this age group has not been considered in the safety assessment.

Infants (0.5-1 years)

Acceptable safety margins are met for infants when considering individual product exposure scenarios for the product types as listed in Table 3a at the stated concentrations. When considering an aggregate exposure scenario (oral + dermal), acceptable safety margins are not met. Hydroalcoholic-based



fragrances, face-make up products, eye make-up products and make-up remover, mouthwash and mouth spray have been excluded from the safety assessment for this age group.

Acceptable safety margins are met for the aggregate exposure scenario when the concentration of methyl salicylate is reduced to either 0.015% in all dermally applied products or 2.5% in toothpaste.

Toddlers (1-3 years)

Acceptable safety margins are met for toddlers when considering individual product exposure and aggregate exposure scenarios for the product types as listed in Table 3b at the stated concentrations. Hydroalcoholic-based fragrances, face-make up products, eye make-up products and make-up remover, mouthwash and mouth spray have been excluded from the safety assessment for this age group.

Children (3-10 years)

3-6 years

Acceptable safety margins are met for children aged 3-6 years old when considering individual product exposure and aggregate exposure scenarios for the product types as listed in Table 3b at the stated concentrations. Hydroalcoholic-based fragrances, face-make up products, eye make-up products and make-up remover, mouthwash and mouth spray have been excluded from the safety assessment for this age group.

6-10 years

For all dermally applied products, acceptable safety margins are met for children aged 6-10 years. Mouthwash use starts at 6 years old so has been included in the safety assessment for this age group. Acceptable safety margins are not met when methyl salicylate is used in mouthwash at a concentration of 0.6%. Consequently, acceptable safety margins are also not met when considering an aggregate exposure scenario (oral + dermal) for ages 6-10 years. Mouth spray has been excluded from the safety assessment for this age group.

Reducing the concentration of methyl salicylate in mouthwash to 0.1% results in acceptable margins of safety for both the individual product and when considering an aggregate scenario.



Adolescents (10-18 years)

10-14 years

Acceptable safety margins are met for adolescents aged 10-14 when considering individual product exposure for the product types listed in Table 3b.

When considering an aggregate exposure scenario (oral + dermal to products in Table 3b), using mean body weights, the margin of safety is greater than 100 at 112. However, members agreed that for the children's safety assessment, P5 body weights should be used instead of the mean body weight so to be appropriately conservative, and protective of the most sensitive populations. The P5 body weight is 29.4kg and represents the 5th percentile for body weight for this age group. In using the P5 body weight and considering an aggregate exposure scenario (oral + dermal to products in Table 3b), for children aged 10-14 years the margin of safety is not acceptable at 88.

Acceptable safety margins are met for the aggregate exposure scenario when the concentration of methyl salicylate in mouthwash is reduced to 0.4%.

14-18 years

Acceptable safety margins are met for this age group when considering both individual and aggregate exposure scenarios as summarised in Table 3b.

Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products

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Summary of Safety Assessment

Table 2)- Adult's exposure

Type of cosmetic product	Maximum concentration	Margin of Safety
<i>Hydroalcoholic-based fragrances</i>	0.600%	5353
<i>Rinse-off skin & hair products (except hand wash products)</i>	0.060%	50332
<i>Hand wash products</i>	0.600%	7508
<i>Leave on skin & hair products (non-aerosol)</i>	0.060%	1203
<i>Face Make up products</i>	0.050%	37975
<i>Lipsticks & lip balm</i>	0.030%	277778
<i>Eye make-up products & make-up remover</i>	0.002%	818777
<i>Toothpaste</i>	2.520%	1375
<i>Mouthwash</i>	0.600%	384
<i>Mouth spray</i>	0.650%	505
<i>Deo spray/aerosol products</i>	0.003%	2273045*
<i>Hair products (spray/aerosol)</i>	0.009%	602697*
<i>Body Lotion Spray</i>	0.040%	785480*
	Aggregate	149 ⁶

*Inhalation exposure, using a different PoD of 154mg/kg bw/day

Table 3a) Infant's exposure

0.5-1 years		
Type of cosmetic product	Maximum concentration	Margin of Safety
<i>Hydroalcoholic-based fragrances</i>	0.02%	n/a
<i>Rinse-off skin & hair products (except hand wash products)</i>	0.02%	87515
<i>Hand wash products</i>	0.02%	131349
<i>Leave on skin & hair products (non-aerosol)</i>	0.02%	2279
<i>Face Make up products</i>	0.02%	n/a
<i>Lipsticks & lip balm</i>	0.02%	219298
<i>Eye make-up products & make-up remover</i>	0.002%	n/a
<i>Toothpaste</i>	2.520%	104
	Aggregate	99.4 ⁶

Excluding the inhalation route (minor route of exposure).

Some cosmetic products are not habitually used by children across certain age groups and therefore have been excluded from the safety assessment. This is denoted by 'n/a' in the table.

The MoS is greater than 100 for total aggregate exposure for infants in the following scenarios (Table 10c):

1. Reduce concentration in toothpaste to 2.5%- MoS=100.2
2. Reduce concentration in all dermally applied products to a maximum of 0.015% -MoS= 100.5

⁶ Calculated as per the SCCS Notes of Guidance (2023b) [SCCS/1647/22](#)



Table 3b) Toddler, children, and adolescent's exposure

Type of cosmetic product	Maximum concentration	Margin of Safety				
		1-3y	3-6y	6-10y	10-14y	14-18y
<i>Hydroalcoholic-based fragrances</i>	0.600%	n/a	n/a	1081	1081	5353
<i>Rinse-off skin & hair products (except hand wash products)</i>	0.060%	27322	29070	8617	8617	50332
<i>Hand wash products</i>	0.600%	4647	4941	21618	21618	7508
<i>Leave on skin & hair products (non-aerosol)</i>	0.060%	807	858	353	353	1203
<i>Face Make up products</i>	0.050%	n/a	n/a	17294	17294	37975
<i>Lipsticks & lip balm</i>	0.030%	155280	164474	574219	574219	277778
<i>Eye make-up products & make-up remover</i>	0.002%	n/a	n/a	400909	400909	818777
<i>Toothpaste</i>	2.520%	129	208	303	636	974
<i>Mouthwash*</i>	0.600%	n/a	n/a	(81)	(170)	260
	0.400%	n/a	n/a	-	255	-
	0.100%	n/a	n/a	186	-	-
<i>Mouth spray</i>	0.650%	n/a	n/a	n/a	n/a	505
	Aggregate⁷	108	161	107	105	124

Excluding the inhalation route (minor route of exposure).

Some cosmetic products are not habitually used by children across certain age groups and therefore have been excluded from the safety assessment. This is denoted by 'n/a' in the table.

*Mouthwash use starts at 6 years. For the age groups 6-10 years and 10-14 years, the MoS values for 0.6% mouthwash are NOT included in the aggregate, instead the MoS values for 0.1% and 0.4% mouthwash (respectively) are included. This is explained in full in Section 5: Conclusions.

⁷ Calculated as per the SCCS Notes of Guidance (2023b) [SCCS/1647/22](#)

Safety Assessment

The full industry dossier, key unpublished studies and other references have been supplied to the committee.

Using the proposed use levels from Table 1 in the main paper, the following exposure and Margin of Safety calculations have been performed. Exposure assessments have used the default values for product use amounts as defined in the SCCS Notes of Guidance (2023b) unless data was unavailable. In this case, an alternative method to estimate daily use amounts is used and will be indicated.

A dermal absorption value of 50% has been applied to all dermally applied products excluding lip products and oral hygiene products, where a value of 100% has been used as a worst-case. Oral absorption is assumed to be 100%.

For dermally applied and oral products, a point of departure of 75 mg/kg bw/day is used based on Collins et al., (1971). For inhalation, a point of departure of 154 mg/kg bw/day is used based on the NOAEL of 700 mg/m³ determined by Gage (1970). Margin of Safety (MoS) is 100 (default).

Summary of safety assessment tables

Dermal

Table 4 Worst case deterministic aggregate Tier 1 exposure assessment (SCCS) for all dermally applied products and oral hygiene products to calculate SED_{dermal} and Margin of Safety (MoS) in adults.

Oral

Table 5 Calculation of SED_{oral} and MoS following oral ingestion of toothpaste by children.

Table 6a Calculation of SED_{oral} and MoS following oral ingestion of mouthwash (0.6%) by children aged 6 years and older.

Table 6b	Calculation of SED_{oral} and MoS following oral ingestion of mouthwash with 0.1% concentration of methyl salicylate by children aged 6-10 years.
Table 6c	Calculation of SED_{oral} and MoS following oral ingestion of mouthwash with 0.4% concentration of methyl salicylate by adolescents aged 10-14 years.
Table 7a	Calculation of SED_{oral} and MoS following the aggregate exposure to toothpaste and mouthwash for children aged 6 years and older.
Table 7b	Calculation of SED_{oral} and MoS following the aggregate exposure to toothpaste and mouthwash (0.1% methyl salicylate) for children aged 6-10 years.
Table 7c	Calculation of SED_{oral} and MoS following the aggregate exposure to toothpaste and mouthwash (0.4% methyl salicylate) for adolescents aged 10-14 years.

Children

Table 8	Calculation of SED_{dermal} and MoS for children aged 6-14 using data from Ficheux and Roudout, (2017) for all dermally applied products (excluding oral hygiene products).
Table 9a	Calculation of SED_{dermal} for children ages 0.5-1, 1-3- and 3-6-years using data from the SCCS notes of guidance (2023b), EFSA (2012a) and Sharkey et al., (2001).
Table 9b	Calculation of aggregate SED_{dermal} from Table 9a and MoS
Table 9c	Calculation of SED_{dermal} and MoS following the individual and aggregate exposure to the dermally applied products detailed below containing the revised concentration of 0.02% methyl salicylate for infants aged 0.5-1 years.
Table 10a	Calculation of aggregate MoS for exposure to oral and dermal products for children using the SED_{oral} and SED_{dermal} aggregate values calculated from P5 body weight data.

Table 10b	Calculation of aggregate MoS for exposure to oral and dermal products for children using the SED_{oral} and SED_{dermal} aggregate values calculated from P5 body weight data using revised concentration limits for methyl salicylate as detailed in Tables 6b, 6c and 9c.
Table 10c	Calculation of an acceptable aggregate MoS for the age group 0.5-1 years
	Inhalation (Adults)
Table 11	Calculation of $SED_{inhalation}$ and MoS for exposure to methyl salicylate from non-spray, dermally applied products using a 1-box model.
Table 12	Calculation of SED_{dermal} and $SED_{inhalation}$ (from residual product on skin) for sprayed products
Table 13	Two-box inhalation model to calculate $SED_{inhalation}$ and MoS for sprayed products.
Table 14	Calculation of aggregate $SED_{inhalation}$ and MoS for all dermally applied products
Table 15	Aggregate exposure from the dermal, inhalation and oral routes.

Dermal

Table 4) Worst case deterministic aggregate Tier 1 exposure assessment (SCCS) for all dermally applied products and oral hygiene products to calculate SED_{dermal} and Margin of Safety (MoS) in adults.

Product category	Individual products	Exposure route	Concentration of methyl salicylate (%)	Retention Factor	$E_{\text{product/bw}}$ (mg/kg bw/day) ¹	Dermal absorption (%) ²	SED_{dermal} (mg/kg bw/day)	MoS ⁴
Rinse-off skin and hair products (excl. hand wash)	Shower gel	Dermal	0.060	0.01	2.79	50	0.000838	89499
	Hair conditioner	Dermal	0.060	0.01	0.67	50	0.000201	373134
	Shampoo	Dermal	0.060	0.01	1.51	50	0.000452	165929
Hand wash soap		Dermal	0.600	0.01	3.33	50	0.009990	7508
Leave-on skin and hair products	Body lotion	Dermal	0.060	1.00	123.20	50	0.036960	2029
	Face cream	Dermal	0.060	1.00	24.14	50	0.007242	10356
	Hand cream	Dermal	0.060	1.00	32.70	50	0.009810	7645
	Deodorant, non-spray	Dermal	0.060	1.00	22.08	50	0.006624	11322
	Hair styling products	Dermal	0.060	0.10	5.74	50	0.001722	43554
Face make-up products	Liquid foundation	Dermal	0.050	1.00	7.90	50	0.001975	37975
Eye make-up and all make-up remover	Make-up remover	Dermal	0.002	0.10	8.33	50	0.000083	903614
	Eyeshadow	Dermal	0.002	1.00	0.33	50	0.000003	25000000
	Mascara	Dermal	0.002	1.00	0.42	50	0.000004	18750000
	Eyeliners	Dermal	0.002	1.00	0.08	50	0.000001	75000000
Hydroalcoholic-based fragrances ⁵		Dermal	0.600	/	4.67	50	0.014010	5353

Lip products	Lipstick, lip salve	Dermal	0.030	1.00	0.90	100	0.000270	277778
Oral care products	Toothpaste	Oral	2.520	0.05	2.17	100	0.054558	1375
	Mouthwash	Oral	0.600	0.10	32.54	100	0.195240	384
	Mouthspray ³	Oral	0.650	1.00	22.86	100	0.148577	505
	Aggregate						0.49	154

SED – Systemic exposure dose

MoS – Margin of safety

1 – The effective exposure to a product category calculated by dividing the calculated daily exposure by the specific body weight of the persons in the study and taking into account the product specific retention factor as in the SCCS Notes of Guidance (2023b).

2 – A dermal absorption factor of 50% is applied in the calculation of SED_{dermal}. For lip products and oral care products, this value is 100%.

3 – Mouth spray is not included in the SCCS Notes of Guidance (2023b). Exposure was therefore estimated by calculating the amount used a day (from expected amount dispensed at 0.08g/use multiplied by frequency of use at 20 uses per day) and dividing by the default body weight of 70kg.

4 – Margin of Safety was calculated by dividing the PoD (75 mg/kg/day) by the SED_{dermal}

5- E_{product} from [SCCS, 2021](#), no retention factor given.

Overall: Margin of Safety is 154 for aggregate exposure to dermally applied products. This is > 100 and therefore, **acceptable**.

Oral

The oral safety assessment focuses on children, given that children are likely to ingest more toothpaste and mouthwash than adults.

Table 5) Calculation of SED_{oral} and MoS following oral ingestion of toothpaste by children.

Age (years)	Concentration of methyl salicylate (%) in toothpaste	Amount used (mg/day) ¹	Methyl salicylate intake per day (mg/day) ²	Retention factor ³	P5 body weight (kg) ⁴	SED _{P5} (mg/kg bw/day)	Mean body weight (kg) ⁴	SED _{mean} (mg/kg bw/day)	MoS (p5) ⁵	MoS (mean) ⁵
0.5-1	2.52	500	5.04	0.4	7.0	0.72	8.8	0.573	104	131
1-3	2.52	500	5.04	0.4	8.7	0.579	11.9	0.424	129	177
3-6	2.52	500	5.04	0.4	14	0.360	23.1	0.218	208	344
6-10	2.52	2750	3.465	0.05	14	0.248	23.1	0.150	303	500
10-14	2.52	2750	3.465	0.05	29.4	0.118	43.4	0.080	636	939
14-18	2.52	2750	3.465	0.05	45	0.077	61.3	0.057	974	1327

SED – Systemic exposure dose

MoS – Margin of safety

1 – For children aged 3-6, it is assumed that a pea-sized amount (0.25g) of toothpaste is used twice a day (SCCNFP, 2003). For children aged older than 6, the amount used is assumed to be that of adults as set out in the SCCS Notes of Guidance (2023b)

2- Calculated as: concentration x amount used per day x retention factor

3 – A retention factor of 0.4 is a conservative value for children aged 6 and under based on SCCP (2005). A value of 0.05 is used for children older than 6 years old based on the SCCS Notes of Guidance (2023b).

4 – P5 and Mean children body weights have been taken from EFSA (2012a).

5 – Margin of Safety was calculated by dividing the PoD (75 mg/kg/day) by the SED_{oral}.

Table 6a) Calculation of SED_{oral} and MoS following oral ingestion of mouthwash (0.6%) by children aged 6 years and older.

Age (years) ¹	Concentration of methyl salicylate (%) in mouthwash	Amount used (mg/day) ²	Methyl salicylate intake per day (mg/day)	Retention factor ²	P5 body weight (kg) ³	SED _{P5} (mg/kg bw/day)	Mean body weight (kg) ³	SED _{mean} (mg/kg bw/day)	MoS (p5) ⁴	MoS (mean) ⁴
6-10	0.6	21620	12.972	0.1	14	0.927	23.1	0.598	81 ⁵	134
10-14	0.6	21620	12.972	0.1	29.4	0.441	43.4	0.309	170	251
14-18	0.6	21620	12.972	0.1	45	0.288	61.3	0.216	260	354

SED – Systemic exposure dose

MoS – Margin of safety

1 – Mouthwash is not recommended for children under 6 years of age.

2 – From the SCCS Notes of Guidance (2023b).

3 – P5 and Mean children body weights have been taken from EFSA (2012a).

4 – Margin of Safety was calculated by dividing the PoD (75 mg/kg/day) by the SED_{oral}.

5- Using P5 body weights as in EFSA (2012a) for the age range **3-10**, an MOS of 81 has been calculated for children aged 6-10 years. This value is <100 and is therefore **NOT ACCEPTABLE**. All other MOS values are **ACCEPTABLE** as they are greater than 100.

Table 6b) Calculation of SED_{oral} and MoS following oral ingestion of mouthwash with 0.1% concentration of methyl salicylate by children aged 6-10 years.

Mouthwash							
Age	Concentration of methyl salicylate (%)	Amount used (mg/day) ¹	Methyl salicylate intake per day (mg/day)	Retention factor ¹	P5 body weight (kg) ²	SED _{P5} (mg/kg bw/day)	MoS (p5) ³
6-10 years	0.1	21620	2.162	0.1	14	0.154	486

SED – Systemic exposure dose

MoS – Margin of safety

1 – From the SCCS Notes of Guidance (2023b)

2 – P5 body weight has been taken from EFSA (2012a)

3 – Margin of Safety was calculated by dividing the PoD (75 mg/kg/day) by the SED_{oral}.

Table 6c) Calculation of SED_{oral} and MoS following oral ingestion of mouthwash with 0.4% concentration of methyl salicylate by adolescents aged 10-14 years.

Mouthwash							
Age	Concentration of methyl salicylate (%)	Amount used (mg/day) ¹	Methyl salicylate intake per day (mg/day)	Retention factor ¹	P5 body weight (kg) ²	SED _{P5} (mg/kg bw/day)	MoS (p5) ³
10-14 years	0.4	21620	8.648	0.1	29.4	0.294	255

SED – Systemic exposure dose

MoS – Margin of safety

1 – From the SCCS Notes of Guidance (2023b)

2 – P5 body weight has been taken from EFSA (2012a)

3 – Margin of Safety was calculated by dividing the PoD (75 mg/kg/day) by the SED_{oral}.

Table 7a) Calculation of SED_{oral} and MoS following the aggregate exposure to toothpaste and mouthwash for children aged 6 years and older.

Aggregate Age (years) ¹	P5 (body weight)				Mean (body weight)			
	SED toothpaste (mg/kg bw/day)	SED mouthwash (mg/kg bw/day)	Total SED (mg/kg bw/day)	MoS (p5) ²	SED toothpaste (mg/kg bw/day)	SED mouthwash (mg/kg bw/day)	Total SED (mg/kg bw/day)	MoS (mean) ²
6-10³	0.248	0.927	1.175	64	0.150	0.562	0.712	105
10-14	0.118	0.441	0.559	134	0.080	0.299	0.379	198
14-18	0.077	0.288	0.365	205	0.057	0.212	0.268	280

SED – Systemic exposure dose

MoS – Margin of safety

1 – Mouthwash is not recommended for children under 6 years of age, so only children aged 6 and older have been considered in this aggregate scenario.

2 – Margin of Safety was calculated by dividing the PoD (75 mg/kg/day) by the SED_{oral}.

3 – For both the P5 and the mean body weights (EFSA, 2012a), the MOS is <100 for the 6-10 age category. This is **NOT ACCEPTABLE** For the 10-14 and 14-18 age categories, the MOS values are >100 which is **ACCEPTABLE**.

Overall: Within the 6-10 age group, MoS values of **<100** have been calculated for mouthwash using P5 bodyweights, and for the aggregate of toothpaste + mouthwash using both P5 and mean bodyweights. For all other age groups, MoS are **acceptable**.

Table 7b) Calculation of SED_{oral} and MoS following the aggregate exposure to toothpaste and mouthwash (0.1% methyl salicylate) for children aged 6-10 years.

Aggregate (oral, using P5 body weight)				
Age	SED toothpaste (mg/kg bw/day)	SED mouthwash (mg/kg bw/day)	Total SED_{oral} (mg/kg bw/day)	MoS¹
6-10 years	0.248	0.154	0.402	186

SED – Systemic exposure dose

MoS – Margin of safety

1 – Margin of Safety was calculated by dividing the PoD (75 mg/kg/day) by the SED_{oral}.

Table 7c) Calculation of SED_{oral} and MoS following the aggregate exposure to toothpaste and mouthwash (0.4% methyl salicylate) for adolescents aged 10-14 years.

Aggregate (oral, using P5 body weights)				
Age	SED toothpaste (mg/kg bw/day)	SED mouthwash (mg/kg bw/day)	Total SED_{oral} (mg/kg bw/day)	MoS¹
10-14 years	0.118	0.294	0.41214966	182

SED – Systemic exposure dose

MoS – Margin of safety

1 – Margin of Safety was calculated by dividing the PoD (75 mg/kg/day) by the SED_{oral}.

Children's safety assessment

Table 8) Calculation of SED_{dermal} and MoS for **children aged 6-14** using data from Ficheux and Roudout, (2017) for all dermally applied products (excluding oral hygiene products).

Product category	Amount used (p95) (g/d)	P5 body weight (EFSA, 2012a) ¹	Retention factor	Eproduct/bw (mg/kg bw/day) ²	Concentration of methyl salicylate (%)	Dermal absorption (%)	SED _{dermal} (mg/kg bw/day)	MoS ³
Shower gel	15	29.4	0.01	5.10204082	0.06	50	0.00153061	49000
Deodorant, non-spray	0.615	29.4	1	20.9183673	0.06	50	0.00627551	11951
Hydroalcoholic fragrance	0.68	29.4	1	23.1292517	0.6	50	0.06938776	1081
Hand wash soap	3.4	29.4	0.01	1.15646259	0.6	50	0.00346939	21618
Liquid Foundation ⁴	0.51	29.4	1	17.34694	0.05	50	0.004337	17294
Make-up Remover ⁴	5	29.4	0.1	17.0068	0.002	50	0.00017	441000
Eye Shadow ⁴	0.02	29.4	1	0.680272	0.002	50	6.8E-06	11025000
Mascara ⁴	0.025	29.4	1	0.85034	0.002	50	8.5E-06	8820000
Eyeliner ⁴	0.005	29.4	1	0.170068	0.002	50	1.7E-06	44100000
Hair styling products ⁴	4	29.4	0.1	13.60544	0.06	50	0.004082	18375
Body lotion (sunscreen)	14.6	29.4	1	496.598639	0.06	50	0.14897959	503
Face cream	3.029	29.4	1	103.027211	0.06	50	0.03090816	2427

Hand cream	2.6	29.4	1	88.4353741	0.06	50	0.02653061	2827
Shampoo	13.6	29.4	0.01	4.62585034	0.06	50	0.00138776	54044
Conditioner	16.7	29.4	0.01	5.68027211	0.06	50	0.00170408	44012
Lip salve	0.0128	29.4	1	0.43537415	0.03	100	0.00013061	574219
Aggregate							0.299	251

SED – Systemic exposure dose

MoS – Margin of safety

1-P5 body weight for 10–14-year-olds (EFSA, 2012a)

2– The E_{product} has been estimated conservatively from data from Ficheux and Roudout, (2017) by using P95 amount used data and P5 body weight data. The study by Ficheux and Roudout, (2017) looked at cosmetic product amounts used by French girls aged between 4 and 14 years old.

3 – Margin of Safety was calculated by dividing the PoD (75 mg/kg/day) by the SED_{dermal} . All MOS values are >100, including the aggregate scenario, which is **ACCEPTABLE**.

4- As no specific use data is available for children for these product categories, adult use amounts from the SCCC Notes of Guidance (2023b) have been used in combination with the P5 body weight for 10-14 year olds. This is likely to be an overestimate of actual children’s exposure and therefore should be appropriately conservative.

Table 9a) Calculation of SED_{dermal} for **children ages 0.5-1, 1-3- and 3-6-years** using data from the SCCS notes of guidance (2023b), EFSA (2012a) and Sharkey et al., (2001).

Product category	Age range (years)	Eproduct/bw (mg/kg bw/day)¹	Concentration of methyl salicylate (%)	Dermal absorption (%)	SED_{dermal} (mg/kg bw/day)	MoS²
Shampoo	0.5-1	3.14	0.06	50	0.000942	79618
	1-3	2.96		50	0.000888	84459
	3-6	2.78		50	0.000834	89928
Hair conditioner	1-3	1.08	0.06	50	0.000324	231481
	3-6	1.01		50	0.000303	247524
Body lotion	0.5-1	223.43	0.06	50	0.067029	1119
	1-3	210.29		50	0.063087	1189
	3-6	197.89		50	0.059367	1263
Face cream	0.5-1	44	0.06	50	0.0132	5682
	1-3	41.41		50	0.012423	6037
	3-6	38.97		50	0.011691	6415
Hand cream	0.5-1	61.71	0.06	50	0.018513	4051
	1-3	58.08		50	0.017424	4304
	3-6	54.66		50	0.016398	4574
Lip products	0.5-1	1.71	0.03	100	0.000513	146199
	1-3	1.61		100	0.000483	155280
	3-6	1.52		100	0.000456	164474
Shower gel	0.5-1	5.43	0.06	50	0.001629	46041
	1-3	5.11		50	0.001533	48924
	3-6	4.81		50	0.001443	51975

Hand soap	0.5-1	5.71	0.6	50	0.01713	4378
	1-3	5.38		50	0.01614	4647
	3-6	5.06		50	0.01518	4941

SED – Systemic exposure dose

MoS – Margin of safety

1 – The E_{product} has been estimated using body surface area and body weight data from EFSA (2012a) based on Sharkey et al., (2001), and using values for daily use and retention factors as in the SCCS Notes of Guidance (2023b).

2 – Margin of Safety was calculated by dividing the PoD (75 mg/kg/day) by the SED_{dermal}. All MOS values are >100 which is **ACCEPTABLE**.

Table 9b) Calculation of aggregate SED_{dermal} from Table 9a and MoS

Age range (years)	0.5-1	1-3	3-6
SED_{dermal} (mg/kg bw/day)	0.11896	0.1123	0.105672
PoD (mg/kg bw/day)	75	75	75
Safe MoS	100	100	100
MoS	630	668	710
	Acceptable	Acceptable	Acceptable

SED – Systemic exposure dose

MoS – Margin of safety

Table 9c) Calculation of SED_{dermal} and MoS following the individual and aggregate exposure to the dermally applied products detailed below containing the revised concentration of 0.02% methyl salicylate for infants aged 0.5-1 years.

Dermally applied products for 0.5-1 years old					
Product category	E_{product}/bw (mg/kg bw/day)¹	Concentration of methyl salicylate (%)	Dermal absorption (%)	SED (mg/kg bw/day)	MoS²
Shampoo	3.14	0.02	50	0.000314	238854
Body lotion	223.43	0.02	50	0.022343	3357
Face Cream	44	0.02	50	0.0044	17045
Hand cream	61.71	0.02	50	0.006171	12154
Lip products	1.71	0.02	100	0.000342	219298
Shower gel	5.43	0.02	50	0.000543	138122
Hand soap	5.71	0.02	50	0.000571	131349
			Aggregate	0.034684	2162

SED – Systemic exposure dose

MoS – Margin of safety

1 – The E_{product} has been estimated using body surface area and body weight data from EFSA (2012a) based on Sharkey et al., (2001), and using values for daily use and retention factors as in the SCCS Notes of Guidance (2023b).

2 – Margin of Safety was calculated by dividing the PoD (75 mg/kg/day) by the SED_{dermal}.

Table 10a) Calculation of aggregate MoS for exposure to oral and dermal products for children using the SED_{oral} and SED_{dermal} aggregate values calculated from P5 body weight data.

Age range (years)	0.5-1	1-3	3-6	6-10	10-14	14-18
SED _{oral} (mg/kg bw/day)	0.72	0.579	0.36	1.175	0.559	0.365
SED _{dermal} (mg/kg bw/day)	0.11896	0.1123	0.1057	0.299	0.299	0.238 ²
SED _{total} (mg/kg bw/day) ¹	0.83896	0.6913	0.4657	1.474	0.858	0.603
PoD (mg/kg bw/day)	75	75	75	75	75	75
Safe MoS	100	100	100	100	100	100
MoS ³	89	108	161	51	87	124
	Not acceptable	Acceptable	Acceptable	Not acceptable	Not acceptable	Acceptable

SED – Systemic exposure dose

MoS – Margin of safety

1 – SED_{total} = SED_{oral} + SED_{dermal}

2- SED_{dermal} for ages 14-18 is taken from Table 2 (for adult exposure) excluding toothpaste and mouthwash which is considered in the SED_{oral}.

3 – Margin of Safety values are <100 for the 6-10- and 10-14-years age groups. The following MOS calculations have also been made using mean bodyweight data (instead of P5 bodyweights) to calculate the SED_{oral}:

6-10, MOS= 75 (**Not acceptable**)

10-14, MOS= 110 (**Acceptable**)

Overall: MOS values of less than 100 have been calculated for the aggregate (dermal + oral) scenario for the age groups 0.5-1 years, 6-10 years, and 10-14 years. Table 10b therefore presents the aggregate scenario using revised concentrations of methyl salicylate for these age groups.

Table 10b) Calculation of aggregate MoS for exposure to oral and dermal products for children using the SED_{oral} and SED_{dermal} aggregate values calculated from P5 body weight data, using revised concentration limits for methyl salicylate as detailed in Tables 6b, 6c and 9c.

Age range (years)	0.5-1*	1-3	3-6	6-10*	10-14*	14-18
SED _{oral} (mg/kg bw/day)	0.72	0.579	0.36	0.402	0.412	0.365
SED _{dermal} (mg/kg bw/day)	0.0347	0.1123	0.1057	0.299	0.299	0.238 ²
SED _{total} (mg/kg bw/day) ¹	0.7547	0.6913	0.4657	0.701	0.711	0.603
PoD (mg/kg bw/day)	75	75	75	75	75	75
Safe MoS	100	100	100	100	100	100
MoS	99.4	108	161	107	105	124
	Not acceptable	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable

SED – Systemic exposure dose

MoS – Margin of safety

1 – SED_{total} = SED_{oral} + SED_{dermal}

2- SED_{dermal} for ages 14-18 is taken from Table 4 (for adult exposure) excluding toothpaste and mouthwash which is considered in the SED_{oral}.

*-indicates changes to the aggregate MoS (from Table 10a) in these age groups

Overall: An MoS value of less than 100 has been calculated for the aggregate (dermal + oral) scenario for the age group 0.5-1 years. All other age groups have acceptable margins of safety. This is when using the revised concentrations of methyl salicylate for some products. A summary of the children’s safety assessment is presented in the main paper in Tables 3a and 3b.

Table 10c) Calculation of an acceptable aggregate MoS for the age group 0.5-1 years

Revised concentrations of methyl salicylate	SED_{oral} (mg/kg bw/day)	SED_{dermal} (mg/kg bw/day)	SED_{total} (mg/kg bw/day)	PoD (mg/kg bw/day)	Safe MoS	MoS
Toothpaste-2.5%	0.714	0.0347	0.7487	75	100	100.2
All dermal products-0.015%	0.72	0.026	0.746	75	100	100.5

The MoS is greater than 100 for total aggregate exposure in the following scenarios:

1. Reduce concentration in toothpaste to 2.5% (SED_{oral}=0.714 and overall MoS=100.2)
2. Reduce concentration in all dermally applied products to a maximum of 0.015% (SED_{dermal}=0.026 and overall MoS= 100.5)

Inhalation

Table 11) Calculation of SED_{inhalation} and MoS for exposure to methyl salicylate from non-spray, dermally applied products using a 1-box model.

Product category: Non-spray products, dermally applied (1- box model)	Individual products	Concentration of methyl salicylate (%)	E_{product/bw} (mg/kg bw/day)¹	Methyl salicylate available for inhalation (mg/kg bw/day)²	SED_{inhalation} (mg/kg bw/day)³	MoS⁴
Rinse-off skin and hair products (excl. hand wash)	Shower gel	0.060	2.79	0.00084	0.000022932	6715507
	Hair conditioner	0.060	0.67	0.00020	0.00000546	28205128
	Shampoo	0.060	1.51	0.00045	0.000012285	12535613
Hand wash soap		0.600	3.33	0.00999	0.000273	564667
Leave-on skin and hair products	Body lotion	0.060	123.20	0.03700	0.00101	152460
	Face cream	0.060	24.14	0.00724	0.00020	779147
	Hand cream	0.060	32.70	0.00981	0.00027	575028
	Deodorant, non- spray	0.060	22.08	0.00662	0.000180726	852119
	Hair styling products	0.060	5.74	0.00172	0.000046956	3279666
Face make-up products	Liquid foundation	0.050	7.90	0.00198	0.000054054	2849003
Eye make-up and all make-up remover	Make-up remover	0.002	8.33	0.00008	0.000002184	70512821
	Eyeshadow	0.002	0.33	3.30E-06	9.009E-08	1709401709
	Mascara	0.002	0.42	4.20E-06	1.1466E-07	1343101343
	Eyeliner	0.002	0.08	8.00E-07	2.184E-08	7051282051
Hydroalcoholic-based fragrances		0.600	4.67	0.01400	0.000382	402930

Lip products	Lipstick, lip salve	0.030	0.90	0.00014	0.000003822	40293040
Total					0.0025	62624

SED – Systemic exposure dose

MoS – Margin of safety

1 – The E_{product} has been estimated as in the SCCS Notes of Guidance (2023b)

2 – Methyl salicylate available for inhalation is the fraction retained on the skin i.e., not absorbed. Based on a dermal absorption of 50%, this is 50% of the applied amount.

3- $SED_{\text{inhalation}}$ has been calculated using the following formula: $SED_{\text{inhalation}} = \text{methyl salicylate available for inhalation (residual, not dermally absorbed)} / \text{room size (10m}^3\text{)} \times \text{time in room (21 minutes)} \times \text{respiration rate (0.013m}^3\text{/min)}$. Room volume is from Bremmer et al., 2006 and Biesebeek et al., 2014. Time in room from RIFM two-box model. Respiration rate from Rothe et al., (2011).

4-The MOS has been calculated by dividing the $POD_{\text{inhalation}}$ (154 mg/kg bw/day) by the $SED_{\text{inhalation}}$. All MOS values calculated are >100 and so are **ACCEPTABLE**.

Table 12) Calculation of SED_{dermal} and SED_{inhalation} (from residual product on skin) for sprayed products

Product type	Concentration methyl salicylate (%)	Daily product use (g/d)¹	Dermal absorption (%)	Retention factor	Proportion of product on skin (%)²	SED_{dermal} (mg/kg bw/day)	SED_{inhalation} from residual product on skin (1-box)⁴
Hydroalcoholic fragrance spray	0.6	0.28	50	1	85	0.0102	N/A
Deodorant spray	0.003	6.1	50	1	11.4	0.000149014	4.068E-06
Hair leave-on spray	0.009	6.8	50	0.1	85	0.000371571	N/A
Body lotion spray	0.04	7.82	50	1	85	0.018991429	0.0005185

SED – Systemic exposure dose

MoS – Margin of safety

1 – From Ficheux and Roudout, (2017), Hall et al., (2007), Steiling et al., (2014) and the SCCS Notes of Guidance (2023b), respectively.

2-The values of 85% for product retained on skin have been taken from Bremmer et al., (2006). The value of 11.4% for deodorant spray has been taken from Steiling et al., (2012).

3-The default body weight of 70kg has been used to calculate SED_{dermal}

4-SED_{inhalation} = (product use (mg/d) x concentration of methyl salicylate x % of methyl salicylate airborne/10m³ x 21 min x 0.013m³/min / 70kg). Not undertaken for hydroalcoholic fragrance spray or hair leave on spray as it is assumed that 100% of the sprayed product is airborne and available for inhalation (worst-case).

Table 13) Two-box inhalation model to calculate $SED_{inhalation}$ and MoS for sprayed products.

	Hydroalcoholic fragrance spray	Deodorant spray	Hair leave-on spray	Body lotion spray
Amount per application (mg/application)	280	3050	5960	7820
Methyl salicylate concentration (%)	0.6	0.003	0.009	0.04
Airbourne fraction (%)¹	100	88.6	100	15
Potential amount inhaled (mg)	1.68	0.08	0.54	0.47
Box 1 Volume (L)²	1000	1000	1000	1000
Duration in box 1 (min)	1	1	1	1
Inhalation rate (L/min)	13	13	13	13
Potential amount inhaled in Box 1	0.0218	0.0011	0.0070	0.0061
Box 2 volume (L)	10000	10000	10000	10000
Duration in box 2 (min)	20	20	20	20
Inhalation rate (L/min)	13	13	13	13
Potential amount inhaled in Box 2	0.0437	0.0021	0.0139	0.0122
Retention fraction in lungs (25% exhaled)³	0.75	0.75	0.75	0.75
Respirable fraction⁴	1	1	1	1
Frequency of application⁵	1	2	1.14	1
Body weight (kg)	70	70	70	70
$SED_{inhalation}$ (mg/kg bw/day)⁶	7.02E-04	6.78E-05	2.56E-04	1.96E-04
POD (mg/kg bw/day)	154	154	154	154

Oral absorption	100	100	100	100
POD_{sys} (mg/kg bw/day)	154	154	154	154
MoS⁷	219373	2273045	602697	785480
Safe MoS	100	100	100	100
Conclusion	Acceptable	Acceptable	Acceptable	Acceptable
Aggregate SED (mg/kg bw/day)	0.001221			
Aggregate MoS	126092	Acceptable		

SED – Systemic exposure dose

MoS – Margin of safety

1 – The value of 88.6% for deodorant spray is taken from Steiling et al., (2012). The value of 15% for body lotion is from Bremmer et al., (2006). Values of 100% have been chosen for HA spray and hair sprays as a worst-case, first-tier assessment.

2 – Box volumes from SCCS Notes of Guidance (2023b)

3- From the SCCS Notes of Guidance (2023b) cited as Rothe et al., (2011)

4-Assumed 1 for all products as a worst-case scenario, due to lack of experimental data

5- From SCCS Notes of Guidance (2023b)

6- $SED_{inhalation} = (\text{Box 1} + \text{Box 2}) \times \text{retention in lungs} \times \text{respirable fraction} \times \text{frequency of application} / \text{body weight (70kg default)}$

7-The MOS has been calculated by dividing the $POD_{inhalation}$ (154 mg/kg bw/day) by the $SED_{inhalation}$. All MOS values calculated are >100 and so are **ACCEPTABLE**.

Table 14) Calculation of aggregate SED_{inhalation} and MoS for all dermally applied products

Product category	Individual products	SED _{inhalation} (mg/kg bw/day)
Rinse-off skin and hair products (excl. hand wash)	Shower gel	2.29E-05
	Hair conditioner	5.46E-06
	Shampoo	1.23E-05
Hand wash soap		0.000273
Leave-on skin and hair products	Body lotion	0.00101
	Face cream	0.0002
	Hand cream	0.00027
	Deodorant, non-spray	0.000181
	Hair styling products SPRAY ¹	0.000256
Face make-up products	Liquid foundation	5.41E-05
Eye make-up and all make-up remover	Make-up remover	2.18E-06
	Eyeshadow	9.01E-08
	Mascara	1.15E-07
	Eyeliner	2.18E-08
Hydroalcoholic-based fragrance SPRAY ¹		0.000702
Lip products	Lipstick, lip salve	3.82E-06
Aggregate (SED mg/kg bw/day)		0.002993
PoDsys (mg/kg bw/day)		154
Safe MoS		100
MoS ²		51454

SED – Systemic exposure dose

MoS – Margin of safety

1 – Hair spray and hydroalcoholic-based fragrance sprays have been included in place of the non-spray equivalents based on higher SED_{inhalation} values calculated.

2 – Margin of Safety >100 is **ACCEPTABLE**

Overall: Methyl salicylate exposure via the inhalation route is low.

Total aggregate scenario

Table 15) Aggregate exposure from the dermal, inhalation and oral routes

Aggregate dermal + inhalation + oral	
Dermal + oral SED (mg/kg/day)¹	0.5003
Inhalation SED (mg/kg/day)²	0.0030
Total SED (mg/kg/day)	0.5033
PoD (mg/kg/day)³	75
MoS	149
	Acceptable

SED – Systemic exposure dose

PoD- Point of Departure

MoS – Margin of safety

1 – Hair spray and hydroalcoholic-based fragrance sprays have been included in place of the non-spray equivalents based on higher SED_{inhalation} values calculated. Dermal exposure from oral hygiene products as in Table 4.

2 – Excludes inhalation from lip products as assumed to be 100% absorbed dermally

3-oralPoD chosen as this is lower than the PoD via the inhalation route

Abbreviations

ADI	Acceptable Daily Intake
CIR	Cosmetics Ingredient Review
CLP	Classification, Labelling and Packaging
CMR	Carcinogenic, Mutagenic and Reprotoxic
EFSA	European Food Safety Authority
FAO	Food and Agriculture Organization of the United Nations
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LOAEL	Lowest Observed Adverse Effect Level
MLC	Mandatory Classification and Labelling
MoS	Margin of Safety
NFSA	Norwegian Food Safety Authority (Mattilsynet)
NOAEL	No Observed Adverse Effect Level
PoD	Point of Departure
QRA	Quantitative Risk Assessment
RAC	European Committee for Risk Assessment
RIFM	Research Institute for Fragrance Materials
SCCNFP	Scientific Committee on Cosmetic and Non-Food Products
SCCP	Scientific Committee on Consumer Products
SCCS	Scientific Committee on Consumer Safety
SED	Systemic Exposure Dose
US-EPA	US-Environmental Protection Agency
WHO	World Health Organization

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