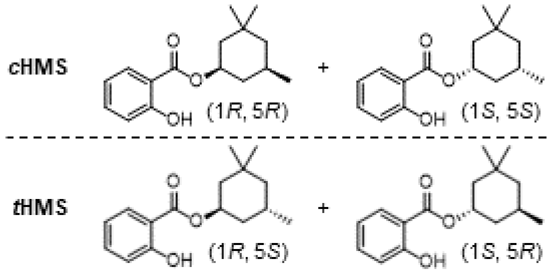
FACTSHEET

Homosalate

Derivation of HBM-I and HBM-II values



Structural formulas of all four homosalate isomers. Pairs of enantiomers are shown on the same side of the dotted line, whilst diastereomers are shown on opposite sides. Graphic adapted from Ebert et al. (2022) [1].

Substance	**Homosalate**		
Year of value derivation	**2026**		
Publication	**Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz** https://doi.org/10.1007/s00103-026-04205-x [2]		
Parameters	**Value / Descriptor**	**Dimension**	**Comment**
HBM values			
HBM-I value (men/children)	HMS-CA5: 0.16 and tHMS-CA: 3.7	µg/L	Matrix: urine Biomarkers: HMS-CA5 and tHMS-CA
HBM-I value (women)	HMS-CA5: 0.14 and tHMS-CA: 3.2	µg/L	
HBM-II value (men/children)	HMS-CA5: 0.49 and tHMS-CA: 11	µg/L	
HBM-II value (women)	HMS-CA5: 0.42 and tHMS-CA: 9.5	µg/L	
General information			
CAS number	118-56-9		
IUPAC name	3,3,5-Trimethylcyclohexyl 2-hydroxybenzoate		
Molar mass homosalate	262.35	g/mol	
HBM biomarkers of exposure	HMS-CA5 and tHMS-CA		Specific metabolites for *cis*-homosalate (HMS-CA5) resp. *trans*-homosalate (tHMS-CA) [3, 4]
Molar mass HMS-CA5 resp. tHMS-CA	292.33	g/mol	
Data base toxicology			
Key study/Author(s) (Year)	[5]		According to OECD guideline 422. Is also a key study in the SCCS's assessment [6]
Species	Wistar rats		10 female and 10 male animals per dose
Method of application/Type of study	Orally via gavage		0, 60, 120, 300 or 750 mg/(kg bw · d) homosalate (Purity 99.8%, dissolved in maize oil)
Duration of exposure	7 weeks		
Critical endpoint/Effect	Increased absolute and relative kidney weights		
LOAEL	60	mg/kg bw/d	= POD
Assessment factors and external dose for deriving HBM values (Based on the SCCS's risk assessment [6])			
Extrapolation from the LOAEL to the NAEL	3		
Time extrapolation	2		Subchronic to chronic [7]
Interspecies factor	4		Allometric
	2.5		Dynamic
Intraspecies factor	10		

Total assessment factor (TAF) für HBM-I	600		
POD/TAF for HBM-I	100	µg/(kg bw · d)	Homosalate
External tolerable dose (ETD) of the stereoisomers for HBM-I	Cis-homosalate: 100 µg/(kg bw · d) · 0.9 = 90 µg/(kg bw · d) Trans-homosalate: 100 µg/(kg bw · d) · 0.1 = 10 µg/(kg bw · d)	µg/(kg bw · d)	The factors 0.9 and 0.1 reflect the ratio of cis- to trans-homosalate in technical homosalate (approx. 90:10)
Total assessment factor (TAF) for HBM-II	200		
POD/TAF for HBM-II	300	µg/(kg bw · d)	Homosalate
External dose of the stereoisomers for HBM-II	Cis-homosalate: 300 µg/(kg bw · d) · 0.9 = 270 µg/(kg bw · d) Trans-homosalate: 300 µg/(kg bw · d) · 0.1 = 30 µg/(kg bw · d)	µg/(kg bw · d)	The factors 0.9 and 0.1 reflect the ratio of cis- to trans-homosalate in technical homosalate (approx. 90:10)
Parameters for calculating HBM values using the mass balance approach			
$Fue_{(48\ h)}$	HMS-CA5: 0.0097% tHMS-CA: 1.0%		Excretion factor, the proportion of the active substance dose excreted in the urine as a specific metabolite, on a molar basis [1]
Difference between the dermal and oral routes ($F_{D/O}$)	HMS-CA5: 0.5 tHMS-CA: not applicable (≈1)		[8]
Ratio of the molar mass of the metabolite to the molar mass of homosalate	HMS-CA5/HMS: 1.11 tHMS-CA/HMS: 1.11		292.33/262.35 = 1.11 292.33/262.35 = 1.11
Urine volume per kg bw per day	Men/Children: 0.030 Women: 0.035	L/(kg bw · d)	Default values [9]
Calculation of HBM values in accordance with the mass balance approach ([7])			
HBM-I value (men/children)	HMS-CA5: 0.16 µg/L and tHMS-CA: 3.7 µg/L	µg/L	**HMS-CA5:** 90 µg/(kg bw · d) · 1.11 · 0.0097% · 0.5/ 0.030 L/(kg bw · d) = 0.16 µg/L **tHMS-CA:** 10 µg/(kg bw · d) · 1.11 · 1.0%/ 0.030 L/(kg bw · d) = 3.7 µg/L
HBM-I value (women)	HMS-CA5: 0.14 µg/L and tHMS-CA: 3.2 µg/L	µg/L	**HMS-CA5:** 90 µg/(kg bw · d) · 1.11 · 0.0097% · 0.5/ 0.035 L/(kg bw · d) = 0.14 µg/L **tHMS-CA:** 10 µg/(kg bw · d) · 1.11 · 1.0%/ 0.035 L/(kg bw · d) = 3.2 µg/L
HBM-II value (men/children)	HMS-CA5: 0.49 µg/L and tHMS-CA: 11 µg/L	µg/L	**HMS-CA5:** 270 µg/(kg bw · d) · 1.11 · 0.0097% · 0.5/ 0.030 L/(kg bw · d) = 0.49 µg/L **tHMS-CA:** 30 µg/(kg bw · d) · 1.11 · 1.0%/ 0.030 L/(kg bw · d) = 11 µg/L
HBM-II value (women)	HMS-CA5: 0.42 µg/L and tHMS-CA: 9.5 µg/L	µg/L	**HMS-CA5:** 270 µg/(kg bw · d) · 1.11 · 0.0097% · 0.5/ 0.035 L/(kg bw · d) = 0.42 µg/L **tHMS-CA:** 30 µg/(kg bw · d) · 1.11 · 1.0%/0.035 L/(kg bw · d) = 9.5 µg/L

Reasoning

Homosalate is marketed under trade names such as Neo Heliopan® HMS, Eusolex® HMS, and Parsol® HMS. Homosalate is a weak UV-B absorber with an absorption maximum at 306 nm; Regulation (EU) 2022/2195 [10] reduced the maximum permitted concentration in ready-to-use preparations to 7.34% and restricted its use to facial products, with the exception of spray products containing propellants. This is accompanied by an amendment to entry 3 in Annex VI to the Cosmetics Regulation (EC) No 1223/2009 [11].

Due to the stereochemistry of the alcohol used, esterification produces a mixture of four stereoisomers, which can be divided into two pairs of diastereomers: cis- and trans-homosalate. For regulatory purposes, this mixture of isomers is treated as a single substance.

An analysis of various current sunscreens and technical HMS revealed cis-homosalate contents of 85–92 per cent [1]. Homosalate is predominantly used in sunscreens; a product screening carried out by the Danish Environment Protection Agency (DEPA) has also identified face creams, make-up and lip care as relevant product groups [12].

The key study used to derive the HBM values was the study conducted in accordance with OECD guideline 422 in rats (oral route) using a mixture of homosalate isomers, which was also used for the risk assessment by the SCCS. The most sensitive endpoint observed here was an increase in absolute and relative kidney weights in males from the lowest dose of 60 mg/(kg bw · d).

This LOAEL was used as point of departure (POD) for deriving the HBM values; in line with the SCCS risk assessment, an assessment factor of 3 was applied to extrapolate from the LOAEL to the NAEL. For the temporal extrapolation (from subchronic to chronic), the approach for deriving the HBM values provides for an additional assessment factor of 2 [7].

Consequently, the external tolerable dose of HMS used to derive HBM-I values (TDI-equivalent value) was calculated as 100 µg/(kg bw · d) by using a total assessment factor of 600 (a factor of 10 each for inter- and intra-species variability, a factor of 3 for the extrapolation from LOAEL to NAEL, a factor of 2 for time extrapolation). Similarly, using the LOAEL as point of departure, the external dose of HMS for deriving HBM-II values was calculated with a total uncertainty factor of 200 (a factor of 10 each for inter- and intra-species variability, and a factor of 2 for time extrapolation) to 300 µg/(kg bw · d).

Separate HBM values were determined for the specific cis-homosalate biomarker (HMS-CA 5) and the specific trans-homosalate biomarker (tHMS-CA). Consequently, external doses for cis- and trans-homosalate were required for further calculations. Given the ratio of cis- to trans- homosalate in technical homosalate of 90:10 (on a molar basis; in this case identical to w/w), the external doses for humans were found to be

a) 90 µg/(kg bw · d) *cis*-homosalate und 10 µg/(kg bw · d) *trans*-homosalate for the calculation of HBM-I values
b) 270 µg/(kg bw · d) *cis*-homosalate und 30 µg/(kg bw · d) *trans*-homosalate for calculation of HBM-II values

References

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