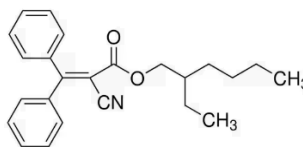


|                                     |                                                                                                                                                                                 |            |                                                                                                                                |
|-------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|--------------------------------------------------------------------------------------------------------------------------------|
| FACTSHEET<br>Octocrylene (OC)       | Update <sup>1</sup> of the derivation of HBM values                                                                                                                             |            |                                                                                                                                |
|                                     |                                                                                               |            |                                                                                                                                |
| Substance                           | Octocrylene                                                                                                                                                                     |            |                                                                                                                                |
| Year of value derivation            | 2023                                                                                                                                                                            |            |                                                                                                                                |
| Update                              | 2026                                                                                                                                                                            |            |                                                                                                                                |
| Underlying publication              | Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz 66<br><a href="https://doi.org/10.1007/s00103-023-03785-2">https://doi.org/10.1007/s00103-023-03785-2</a> [1] |            |                                                                                                                                |
| Parameters                          | Value / Descriptor                                                                                                                                                              | Dimension  | Comment                                                                                                                        |
| HBM values CPAA                     |                                                                                                                                                                                 |            |                                                                                                                                |
| HBM-I value (men/children)          | 5.3                                                                                                                                                                             | mg/L       | Matrix: urine<br>Biomarker CPAA (2-cyano-3,3-diphenylacrylic acid)                                                             |
| HBM-I value (women)                 | 4.5                                                                                                                                                                             | mg/L       |                                                                                                                                |
| HBM-II value (men/children)         | 18                                                                                                                                                                              | mg/L       |                                                                                                                                |
| HBM-II value (women)                | 16                                                                                                                                                                              | mg/L       |                                                                                                                                |
| HBM values DOCCA                    |                                                                                                                                                                                 |            |                                                                                                                                |
| HBM-I value (men/children)          | 22                                                                                                                                                                              | µg/L       | Matrix: urine<br>Biomarker DOCCA (2-(carboxymethyl) butyl 2-cyano-3,3-diphenylacrylate; Dinor-OC-carboxylic acid)              |
| HBM-I value (women)                 | 19                                                                                                                                                                              | µg/L       |                                                                                                                                |
| HBM-II value (men/children)         | 78                                                                                                                                                                              | µg/L       |                                                                                                                                |
| HBM-II value (women)                | 67                                                                                                                                                                              | µg/L       |                                                                                                                                |
| General information                 |                                                                                                                                                                                 |            |                                                                                                                                |
| CAS number                          | 6197-30-4                                                                                                                                                                       |            |                                                                                                                                |
| IUPAC name                          | 2-ethylhexyl-2-cyano-3,3-diphenylacrylate                                                                                                                                       |            |                                                                                                                                |
| Molar mass Octocrylene              | 361.48                                                                                                                                                                          | g/mol      |                                                                                                                                |
| HBM biomarker of exposure           | CPAA<br>DOCCA                                                                                                                                                                   |            | Specific metabolites                                                                                                           |
| Molar mass of metabolites           | CPAA: 249.27<br>DOCCA: 363.41                                                                                                                                                   | g/mol      |                                                                                                                                |
| Data base toxicology                |                                                                                                                                                                                 |            |                                                                                                                                |
| Key study/Author(s) (Year)          | Triskelion BV, 2019                                                                                                                                                             |            | [2]                                                                                                                            |
| Species                             | Rat                                                                                                                                                                             |            |                                                                                                                                |
| Method of application/Type of study | Oral (feed)                                                                                                                                                                     |            | OECD guideline 443                                                                                                             |
| Duration of exposure                | Extended One-Generation Reproductive Toxicity Study (EOGRTS)                                                                                                                    |            | During the mating season (10 weeks) and the mating period (max. 2 weeks), pregnancy and lactation up to the 21st postnatal day |
| Critical endpoint/Effect            | Systemic toxicity, reproductive and developmental toxicity                                                                                                                      |            |                                                                                                                                |
| NOAEL<br>LOAEL                      | 153<br>534                                                                                                                                                                      | mg/kg bw/d | POD for HBM-I values<br>POD for HBM-II values                                                                                  |

<sup>1</sup> The HBM values were updated on the basis of updated daily urine volumes normalised for body weight, and by systematically rounding the calculated values.

| Assessment factors and external dose for deriving HBM values                 |                                                            |                |                                                                                                                                        |
|------------------------------------------------------------------------------|------------------------------------------------------------|----------------|----------------------------------------------------------------------------------------------------------------------------------------|
| Adjusted exposure factor (time scaling)                                      | 2                                                          |                | Any potential amplification of effects due to exposure over lifetime must be taken into account                                        |
| Interspecies factor                                                          | 4                                                          |                | Allometric                                                                                                                             |
|                                                                              | 2.5                                                        |                | Dynamic                                                                                                                                |
| Intraspecies factor                                                          | 5                                                          |                | General population, kinetic + dynamic; reduced from 10 to 5, as EOGRTS covers the particular sensitivity during development            |
| Other assessment factors: Quality of the data as a whole                     | 3                                                          |                | Taking into account uncertainties relating to the results of the mechanistic study [3]                                                 |
| Total assessment factor (TAF)                                                | 300                                                        |                |                                                                                                                                        |
| POD/TAF                                                                      | For HBM-I: 0.51<br>For HBM-II: 1.78                        | mg/kg bw/d     | External tolerable dose (ETD) for the HBM-I value: $153/300 = 0.51$<br>External dose for the HBM-II value: $534/300 = 1.78$            |
| Parameters for calculating HBM values using the mass balance approach        |                                                            |                |                                                                                                                                        |
| Fue                                                                          | CPAA: 45% = 0.45<br>DOCCA: 0.13% = 0.0013                  |                | Urinary excretion fraction, proportion of the active substance dose excreted in urine as a specific metabolite, on a molar basis [4,5] |
| Ratio of the molar mass of the metabolite to the molar mass of octocrylene   | For CPAA: 0.69<br>For DOCCA: 1.01                          |                | 249.27/362.48<br>363.41/362.48                                                                                                         |
| Urine volume per kg bw per day                                               | Men/Children: 0.030<br>Women: 0.035                        | L/ (kg bw · d) | Default values [6]                                                                                                                     |
| Calculation of HBM values in accordance with the mass balance approach ([7]) |                                                            |                |                                                                                                                                        |
| CPAA                                                                         |                                                            |                |                                                                                                                                        |
| HBM-I value (men/children)                                                   | Rounded value: 5.3                                         | mg/L           | $[0.51 \times 0.69 \times 0.45] / 0.030$                                                                                               |
| HBM-I value (women)                                                          | Rounded value: 4.5                                         | mg/L           | $[0.51 \times 0.69 \times 0.45] / 0.035$                                                                                               |
| HBM-II value (men/children)                                                  | Rounded value: 18                                          | mg/L           | $[1.78 \times 0.69 \times 0.45] / 0.030$                                                                                               |
| HBM-II value (women)                                                         | Rounded value: 16                                          | mg/L           | $[1.78 \times 0.69 \times 0.45] / 0.035$                                                                                               |
| DOCCA                                                                        |                                                            |                |                                                                                                                                        |
| HBM-I value (men/children)                                                   | Rounded value: 0.022 mg/L<br>$\triangleq 22 \mu\text{g/L}$ |                | $[0.51 \times 1.01 \times 0.0013] / 0.030$                                                                                             |
| HBM-I value (women)                                                          | Rounded value: 0.019 mg/L<br>$\triangleq 19 \mu\text{g/L}$ |                | $[0.51 \times 1.01 \times 0.0013] / 0.035$                                                                                             |
| HBM-II value (men/children)                                                  | Rounded value: 0.078 mg/L<br>$\triangleq 78 \mu\text{g/L}$ |                | $[1.78 \times 1.01 \times 0.0013] / 0.030$                                                                                             |
| HBM-II value (women)                                                         | Rounded value: 0.067 mg/L<br>$\triangleq 67 \mu\text{g/L}$ |                | $[1.78 \times 1.01 \times 0.0013] / 0.035$                                                                                             |

## Reasoning

Octocrylene (OC) is used as a UV filter in sunscreens due to its UV-absorbing properties in the UVB and UVA ranges, usually in combination with other UV filters. Furthermore, due to its photostability, it is used as a stabiliser for other non-photostable UV filters in sunscreens and cosmetics, or as a photostabiliser for other products (e.g. plastics).

The Extended One-Generation Reproductive Toxicity Study (EOGRTS) [2] is regarded as a key study for assessing the toxicity of OC, and the NOAEL (*No Observed Adverse Effect Level*) of 153 mg/kg body weight per day for systemic, reproductive and developmental toxicity was used as the starting point

(POD - *Point Of Departure*) for deriving HBM-I values. The LOAEL (*Lowest Observed Adverse Effect Level*) from the EOGRTS, amounting to 534 mg/kg bw/day, served as the basis for deriving HBM-II values. A mechanistic subacute feeding study in Wistar rats [3] was used as supporting study.

Taking into account an overall assessment factor of 300, a TDI-equivalent value (TDI: *Tolerable Daily Intake*) of 0.51 mg/kg bw/day was calculated based on the NOAEL to derive the HBM-I values, and an external dose of 1.78 mg/kg bw/day was calculated to derive the HBM-II values.

The OC metabolites CPAA (ester hydrolysis product 2-cyano-3,3-diphenylacrylic acid) with a F<sub>ue</sub> of 45 % and DOCCA (beta-oxidation product 2-(carboxymethyl)butyl 2-cyano-3,3-diphenyl acrylate (dinor-OC-carboxylic acid)) with a F<sub>ue</sub> of 0.13 % are the exposure biomarkers relevant to human biomonitoring [4,5].

Based on the PODs and assessment factors set out above, HBM-I and HBM-II values were derived and agreed upon separately for the biomarkers CPAA and DOCCA.

For the **CPAA biomarker**, HBM-I values of 5.3 mg/L were derived for children and men, and 4.5 mg/L for women. The HBM-II value is 18 mg/L for children and men, and 16 mg/L for women.

For the **DOCCA biomarker**, the HBM-I values are 22 µg/L for children and men, and 19 µg/L for women. The HBM-II value is 78 µg/L for children and men, and 67 µg/L for women.

## References

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2. Triskelion BV (2019) Extended One Generation Reproductive Toxicity Study (EOGRTS) according OECD Test Guideline 443. Testing laboratory: Triskelion BV, Report no: 03R0495/00X056, Owner company: BASF SE; DSM
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4. Bury D, Belov VN, Qi Y, Hayen H, Volmer DA, Brüning T, Koch HM (2018) Determination of urinary metabolites of the emerging UV filter octocrylene by online-SPE-LC-MS/MS. Anal Chem 90(1): 944–951. <https://doi.org/10.1021/acs.analchem.7b03996>
5. Bury et al (2019) Urinary metabolites of the UV filter octocrylene in humans as biomarkers of exposure. Arch Toxicol 93(5): 1227–1238
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7. Kommission Human-Biomonitoring des Umweltbundesamtes (2014) Grundsatzpapier zur Ableitung von HBM-Werten. Stellungnahme der Kommission Human-Biomonitoring des Umweltbundesamtes. Bundesgesundheitsbl Gesundheitsforsch Gesundheitsschutz 57(1):138-147. <http://link.springer.com/article/10.1007/s00103-013-1867-2>