

Submission by the Endocrine Society to the European Chemicals Agency (ECHA) Consultation on the identification of (±)-1,7,7-trimethyl-3-[(4-methylphenyl)methylene]bicyclo[2.2.1]heptan-2-one (4-MBC) as a substance of very high concern (SVHC) due to endocrine disrupting properties.

October 15, 2021

Comments on the identity of the substance (Part I, section 1 of the Annex XV SVHC report) and on the proposed SVHC property / properties (Part I, sections 3-6):

The Endocrine Society appreciates the opportunity to comment on the identification of 4-MBC as a SVHC due to its endocrine disrupting properties. Decades of research and peer-reviewed scientific studies, including many published in the Endocrine Society's journals and cited in the report, have elucidated the hazardous properties of 4-MBC on endocrine systems. We commend the authors of the report for preparing a detailed and careful evaluation of the effects of 4-MBC on estrogen and thyroid biology, with consequent linkages to important health effects including neurodevelopment and sub/infertility. We support the conclusion on page 9 that 4-MBC meets the criteria of Article 57(f) of REACH due to endocrine disrupting properties for which there is scientific evidence of probable serious effects to human health. We also share the authors' concern that it may be difficult to establish a safe level of 4-MBC given the likelihood of effects on the endocrine system, which may occur at extremely low doses, with mixture effects, and with the potential for low-dose and/or non-monotonic dose responses.

Additional evidence of the effects of 4-MBC has been published in recent months which further supports the conclusions of this report. Below, we cite several recent studies that provide additional information on the ability of 4-MBC to disrupt endocrine systems.

- López-Rodríguez D, et al., [Multi- and Transgenerational Outcomes of an Exposure to a Mixture of Endocrine-Disrupting Chemicals \(EDCs\) on Puberty and Maternal Behavior in the Female Rat](#). Environ Health Perspect. 2021 Aug; 129(8): 087003.
- Liang M, et al., [3-\(4-Methylbenzylidene\) camphor induced reproduction toxicity and antiandrogenicity in Japanese medaka \(*Oryzias latipes*\)](#). Chemosphere. 2020 Jun;249:126224. doi: 10.1016/j.chemosphere.2020.126224. Epub 2020 Feb 14.
- Santonocito M, et al., [Stress under the sun: Effects of exposure to low concentrations of UV-filter 4- methylbenzylidene camphor \(4-MBC\) in a marine bivalve filter feeder, the Manila clam *Ruditapes philippinarum*](#). Aquat Toxicol. 2020 Apr;221:105418. doi: 10.1016/j.aquatox.2020.105418. Epub 2020 Feb 3.
- O'Malley E, et al., [Annual release of selected UV filters via effluent from wastewater treatment plants in Australia](#). Chemosphere. 2020 May;247:125887. doi: 10.1016/j.chemosphere.2020.125887. Epub 2020 Jan 10.



- Lambert FN, et al., [Effects of ultraviolet-filters on Daphnia magna development and endocrine-related gene expression](#). *Aquat Toxicol.* 2021 Jul 17;238:105915. doi: 10.1016/j.aquatox.2021.105915. Online ahead of print.
- Quintaneiro C, et al., [Toxicity effects of the organic UV-filter 4-Methylbenzylidene camphor in zebrafish embryos](#). *Chemosphere.* 2019 Mar;218:273-281. doi: 10.1016/j.chemosphere.2018.11.096. Epub 2018 Nov 15.