

ASPARTAME, METHYLEUGENOL, AND ISOEUGENOL

VOLUME 134

This publication represents the views and expert opinions of an IARC Working Group on the Identification of Carcinogenic Hazards to Humans, which met in Lyon, France, 6–13 June 2023

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IARC MONOGRAPHS
ON THE IDENTIFICATION
OF CARCINOGENIC HAZARDS
TO HUMANS

PRELIMINARY GENERAL REMARKS

This first monograph of the one-hundred-and-thirty-fourth volume of the *IARC Monographs* contains the evaluation of the carcinogenic hazard to humans of aspartame. The other monographs in this volume will be methyleugenol and isoeugenol.

Methyleugenol was considered previously by the *IARC Monographs* programme in 2011 ([IARC, 2013](#)), when it was evaluated as *possibly carcinogenic to humans* (Group 2B). Aspartame and isoeugenol have not been evaluated previously by the *IARC Monographs* programme.

The Advisory Group to Recommend Priorities for the *IARC Monographs* that met in 2019 recommended that all three agents be evaluated with high priority ([IARC, 2019a](#); [Marques et al., 2019](#)). A summary of the findings of this volume appears in *The Lancet Oncology* ([Riboli et al., 2023](#)).

Coordination between the *IARC Monographs* programme and WHO/JECFA for the evaluation of aspartame

The present monograph on aspartame is the result of a highly coordinated effort undertaken within WHO. Firstly, IARC evaluated the carcinogenic hazard of aspartame. Subsequently,

JECFA, the Joint FAO/WHO Expert Committee on Food Additives, conducted a risk assessment for cancer and other noncommunicable diseases, including reviewing and updating the acceptable daily intake (ADI) and dietary exposure assessment for aspartame. The present monograph reports the results of the IARC evaluation of aspartame for cancer hazard identification; the results of the JECFA review of aspartame for dietary exposure and risk assessment have been published separately ([JECFA, 2024](#)).

In line with the procedures established for communication and collaboration between the *IARC Monographs* programme and other WHO programmes, the *IARC Monographs* Meeting 134 on 6–13 June was followed closely by the JECFA Ninety-sixth Meeting on 27 June to 6 July ([JECFA, 2024](#)). Aspartame was evaluated for the first time by IARC and the third time by JECFA. The two bodies conducted independent but complementary reviews of all the available scientific literature. To ensure continuity and exchange of relevant information, three WHO scientists from the JECFA programme (Drs Sanaa and Montez, and Mr Petersen) joined the IARC/WHO Secretariat for the *IARC Monographs* meeting, and two scientists from the *IARC Monographs* programme (Drs Madia and Benbrahim-Tallaa) joined the WHO Secretariat for the JECFA meeting.

Furthermore, three of the seven Observers attending the IARC meeting (Drs Agudo, Barlow, and Wu) also served as members of the expert committee at the JECFA Ninety-sixth Meeting, and relevant literature search results were shared between the two programmes as permitted by any confidentiality requirements.

Scope of the systematic review

Standardized searches of the PubMed database (NCBI, 2023) were conducted for aspartame for each outcome (cancer in humans, cancer in experimental animals, and mechanistic evidence, including the key characteristics of carcinogens). For cancer in humans, searches were also conducted in the Web of Science (Clarivate, 2023) and Embase (Elsevier, 2023) databases. The literature tree for aspartame, including the full set of search terms for the agent name and each outcome type, is available online.¹

As described in the current Preamble to the *IARC Monographs* (last revised in 2019; IARC, 2019b), the Working Group reviews publicly available scientific data, such as peer-reviewed papers in the scientific literature, and may also review unpublished reports, if made available in their final form by governmental agencies and if they contain enough detail for critical review. In the case of aspartame, the Working Group was able to consult and review literature derived from the Call for Data in 2011 for the European Food Safety Authority (EFSA) risk assessment, which was made available and accessible on the EFSA website (EFSA, 2011). In addition, IARC opened a public Call for Data on its website 1 year ahead of the meeting for Volume 134. Eligible studies are only those published or accepted for publication in the openly available scientific literature by the time of the Working Group meeting.

References

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¹ The literature tree for the present monograph is available at: <https://hawcproject.iarc.who.int/assessment/680/> (aspartame).