IARC MONOGRAPHS NEWS

A newsletter from the *IARC Monographs* programme

July
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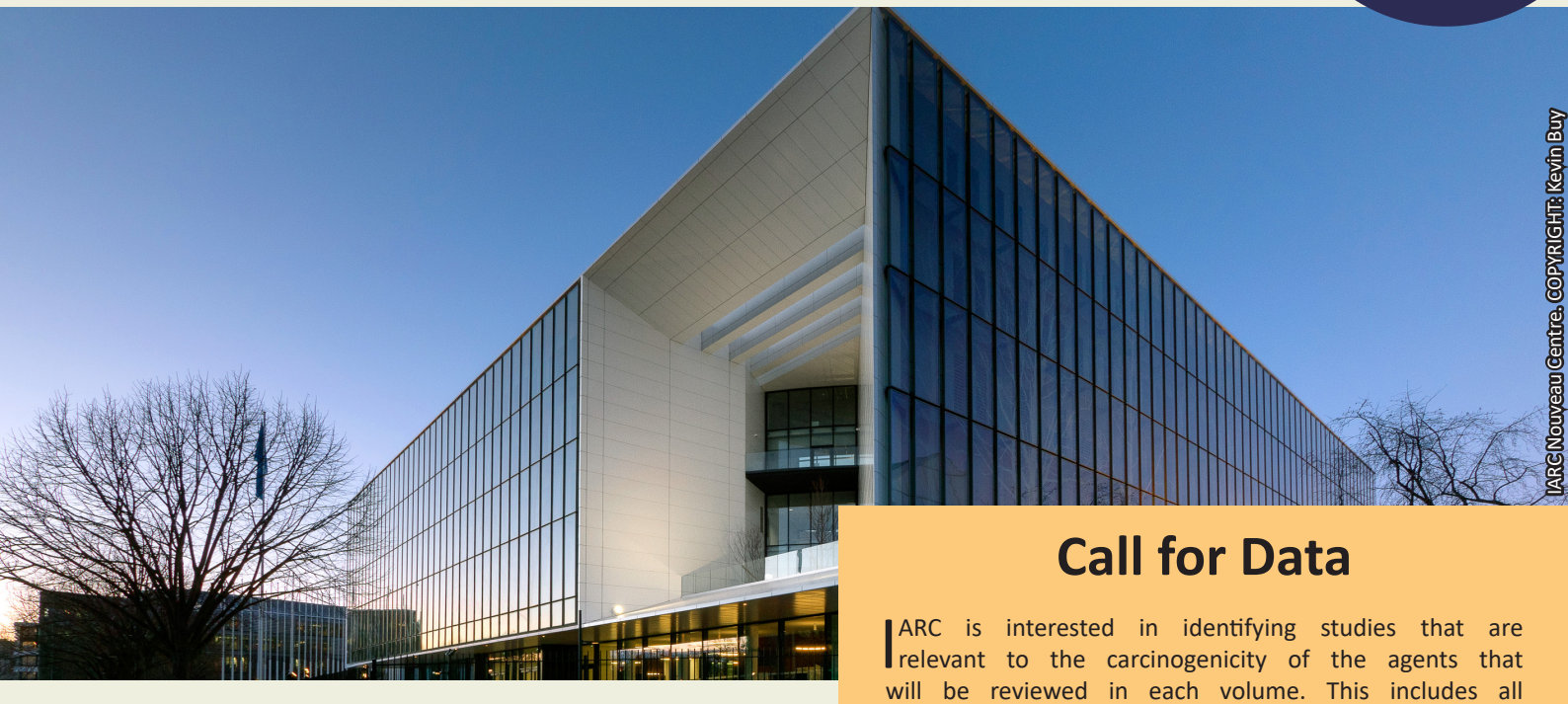


IARC Nouveau Centre. COPYRIGHT: Kevin Buy

The evaluation of aspartame: a WHO collaboration

On 14 July 2023, the World Health Organization (WHO) released the results of a comprehensive evaluation of the artificial sweetener aspartame by two of its bodies, the *IARC Monographs* Programme and the Joint FAO/WHO Expert Committee on Food Additives (JECFA).

A highly coordinated effort was undertaken to evaluate the carcinogenic hazard of aspartame (by IARC) followed by a risk assessment for cancer and other non-communicable diseases, including reviewing and updating the acceptable daily intake (ADI) and dietary exposure assessment for aspartame (by JECFA). In line with the procedures established for communication and collaboration between IARC and other WHO programmes, *IARC Monographs* Meeting 134 on 6–13 June was followed closely by the JECFA Ninety-sixth Meeting on 27 June to 6 July. 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. The most informative studies of cancer in humans were published in 2016–2022. The results of both evaluations were communicated jointly in a press release and an accompanying briefing document (see page 2).

Call for Data

IARC is interested in identifying studies that are relevant to the carcinogenicity of the agents that will be reviewed in each volume. This includes all pertinent cancer epidemiology studies, cancer bioassays, and mechanistic evidence in both exposed humans and experimental systems. Eligible studies should be published or accepted for publication in the openly available scientific literature. Relevant exposure data (particularly from low- and middle-income countries) that are or can be made publicly available are also requested. Please see the *IARC Monographs* Preamble for details of the types of study that may be reviewed.

The **Call for Data** and **Call for Experts** are announced approximately 1 year before the meeting on the *IARC Monographs* website.

Meeting 135: Perfluorooctanoic acid (PFOA) and Perfluorooctanesulfonic acid (PFOS)

Meeting dates: 7–14 November 2023

Call for Data closing date: 7 October 2023

Call for Experts CLOSED 28 November 2022

Meeting 136: Talc and Acrylonitrile

Meeting dates: 11–18 June 2024

Call for Data closing date:10 May 2024

Call for Experts closing date: 31 July 2023

Advisory Group to Recommend Priorities for the *IARC Monographs* during 2025–2029

Meeting dates: 19–22 March 2024

Call for Nomination of Agents closing date: 30 November 2023

Call for Experts closing date: 31 July 2023

IARC encourages the participation of Representatives of national and international health agencies. If you are interested in serving as a Representative, contact us at imonews@iarc.who.int.

International Agency for Research on Cancer

World Health Organization

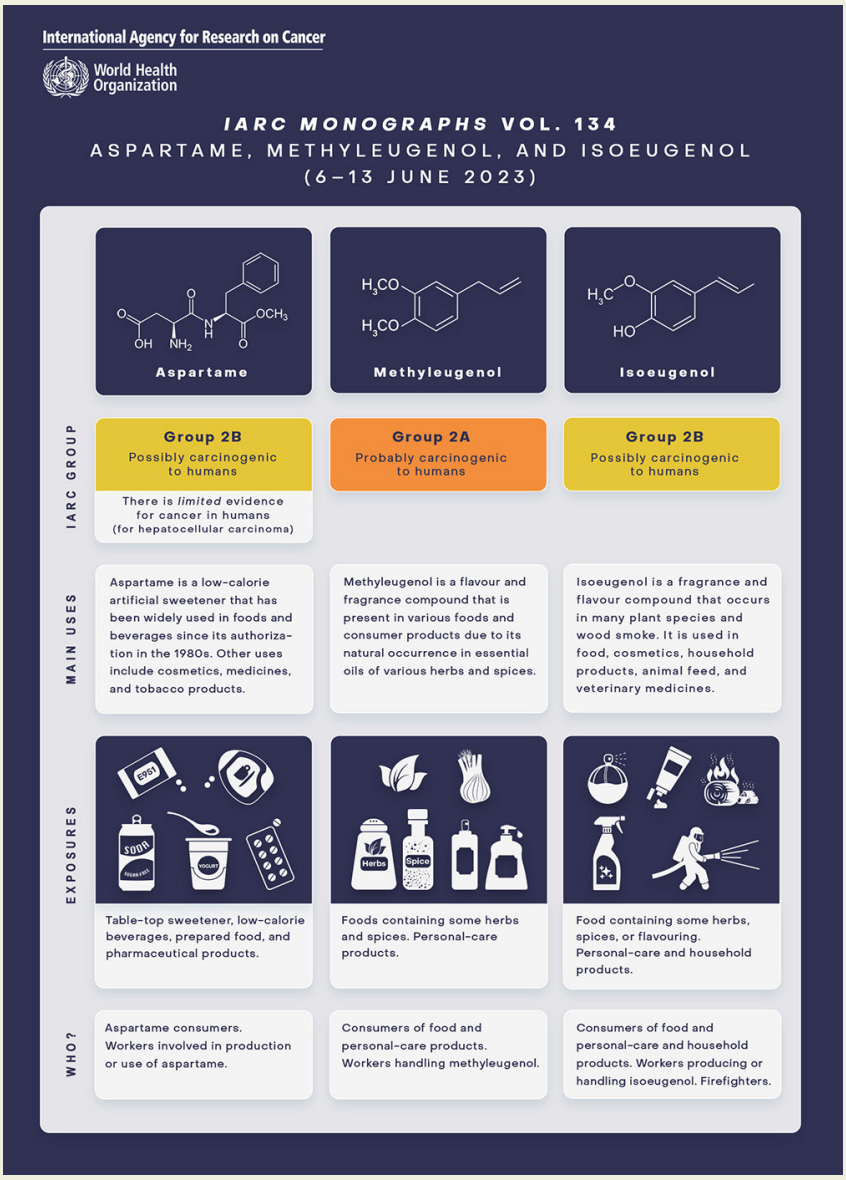
Results of *IARC Monographs* Meeting 134: Aspartame, methyleugenol, and isoeugenol, and JECFA evaluation of aspartame

Meetings held in Lyon on 6–13 June 2023, and Geneva, 27 June to 6 July 2023

IARC classified methyleugenol as *probably carcinogenic to humans* (Group 2A) and isoeugenol as *possibly carcinogenic to humans* (Group 2B) on the basis of *sufficient* evidence for cancer in experimental animals and *inadequate* evidence regarding cancer in humans, together with mechanistic evidence that was *strong* for methyleugenol and *inadequate* for isoeugenol (see Q&A).

IARC classified aspartame as *possibly carcinogenic to humans* (Group 2B) on the basis of *limited* evidence for cancer in humans (specifically, for hepatocellular carcinoma). There was also *limited* evidence for cancer in experimental animals and *limited* mechanistic evidence related to the key characteristics of carcinogens.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) concluded that, although some positive findings were observed for cancer in humans and in experimental animals exposed orally to aspartame, the findings were not sufficiently conclusive to result in a change to the previously established ADI of 0–40 mg/kg body weight. WHO/JECFA and IARC highlight the need for more research to refine the understanding of whether aspartame poses a carcinogenic hazard or risk of other chronic diseases, such as diabetes. The results are consistent with the overall WHO recommendation to reduce intake of sugar and other natural and artificial sweeteners.



Click to enlarge

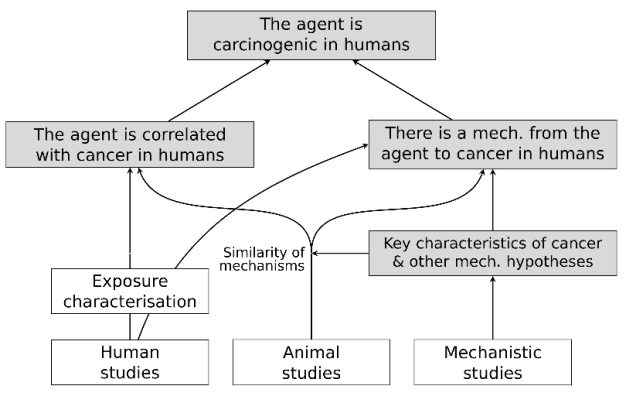
A summary of the results of *IARC Monographs* Meeting 134 has been published in *The Lancet Oncology*.

For more information on the results of both evaluations, see IARC Featured News.

Evidential pluralism and IARC

We are philosophers at the University of Kent who have been discussing evidence assessment with IARC.

Evidential pluralism (EP) is a philosophical theory of causal enquiry that has been developed over the last 15 years [1]. EP encompasses two key claims. The first, *object pluralism*, says that establishing that A is a cause of B (e.g. that exposure to a particular agent causes cancer) requires establishing both that A and B are appropriately correlated and that there must be some mechanism that appeals to A to explain B and that can account for the extent of the correlation. The second, *study pluralism*, maintains that determining whether A is a cause of B requires assessing both association studies (studies that repeatedly measure A and B, together with potential confounders, to quantify their association) and mechanistic studies (studies of features of the mechanisms linking A to B), where available.



Evidence pluralism and IARC evaluations
From [3]

Our previous collaborative work showed that EP accords well with the *IARC Monographs* evaluation process [2, 3] and has informed revisions to the *IARC Monographs* Preamble.

We argued that EP should be more widely employed in medicine, where it leads to a development of evidence-based medicine (EBM) that we call EBM+ [2]. Perhaps EBM+ would have given better outcomes in the COVID-19 pandemic than did EBM, for example [4, 5, 6]. We have also argued that EP can be fruitfully applied to the social sciences [7].

EP also has implications concerning the role of expert consensus conferences, such as the Working Group Meetings held by the *IARC Monographs* programme. It is typically assumed that such conferences help to resolve controversies, in this case, whether exposure to a particular agent causes cancer.

However, it has been argued that consensus conferences are unnecessary for resolving such controversies: an EBM-style analysis of the available studies is sufficient and the conference itself is merely a social ritual [8]. EP reveals the flaw in this argument. Once we recognize the need to assess both association studies and mechanistic studies, we see that an expert consensus conference may be required to resolve controversy. Why? It is a matter of domain expertise. At the outset of a conference, panellists (i.e. Working Group Members) will usually not be in a position to recognize the import of the whole evidence base: the association-study experts will usually not be able to determine the significance of the mechanistic studies and vice versa. Expert group deliberation at a conference is a key way to learn the significance of studies outside of the individual's domain of expertise. It is for this reason that expert consensus conferences help to rationally resolve controversies.

Thus EP offers some interesting philosophical justification for IARC evaluation methods.

If you would like to hear more or get involved, you can contact us at: j.williamson@kent.ac.uk.

Michael Wilde & Jon Williamson
(Philosophy Department, University of Kent)

1. Williamson J (2013). Evidential pluralism [blog]. Kent, UK: University of Kent. Available from: https://blogs.kent.ac.uk/jonw/ep/, accessed 17 May 2023.

2. Parkkinen V-P, Wallmann C, Wilde M, et al. (2018). Evaluating evidence of mechanisms in medicine. Principles and procedures. Springer Cham. Available from: https://link.springer.com/book/10.1007/978-3-319-94610-8

3. Williamson J (2019). Evidential proximity, independence, and the evaluation of carcinogenicity. J Eval Clin Pract. 25(6):955–61. https://doi.org/10.1111/jep.13226

4. Aronson JK, Auker-Howlett D, Ghiara V, et al. (2021). The use of mechanistic reasoning in assessing coronavirus interventions. J Eval Clin Pract. 27(3):684–93. https://doi.org/10.1111/jep.13438

5. Greenhalgh T, Fisman D, Cane DJ, et al. (2022). Adapt or die: how the pandemic made the shift from EBM to EBM+ more urgent. BMJ Evid Based Med. 27(5):253–60. https://doi.org/10.1136/bmjebm-2022-111952

6. Maziarz M, Stencel A (2022). The failure of drug repurposing for COVID-19 as an effect of excessive hypothesis testing and weak mechanistic evidence. Hist Philos Life Sci. 44(4):47. https://doi.org/10.1007/s40656-022-00532-9

7. Shan Y, Williamson J (2023). Evidential pluralism in the social sciences. 1st ed. Routledge. https://doi.org/10.4324/9781003143000

8. Solomon M (2015). Making medical knowledge. Oxford University Press. https://doi.org/10.1093/acprof:oso/9780198732617.001.0001

IARC Monographs exhibition

An exhibition was displayed at the last meeting of the IARC Governing Council and the inauguration of the new IARC headquarters in Gerland, in May 2023. This exhibit presented the breadth of the work of the *IARC Monographs* programme by highlighting a selection of agents that have been evaluated for their potential to cause cancer in humans and some of the public health impact these evaluations have had globally.

Panels were developed on ultraviolet tanning devices, tobacco smoking, outdoor air pollution, asbestos, opium consumption, and occupational exposure as a firefighter.

Other panels presented the *IARC Monographs* Preamble, the distinction between hazard and risk, the process for agent selection, and information on how to nominate agents for prioritization at the March 2024 Advisory Group meeting (see page 5).

A digital version of the exhibition is also available on our website (in English and in French).

The Team

Introducing Niree Kraushaar and Heidi Mattock

Where are you originally from?

NK: I am one of the resident Antipodeans – from Sydney, Australia.

HM: I was born and raised in London, England.

How long have you been at IARC?

NK: I have been at IARC for just over two years now.

HM: I have been here for 14 years, 11 of those with the *IARC Monographs*, but I first discovered IARC as a student in 2000 and always hoped to come back.

What is your role in the team?

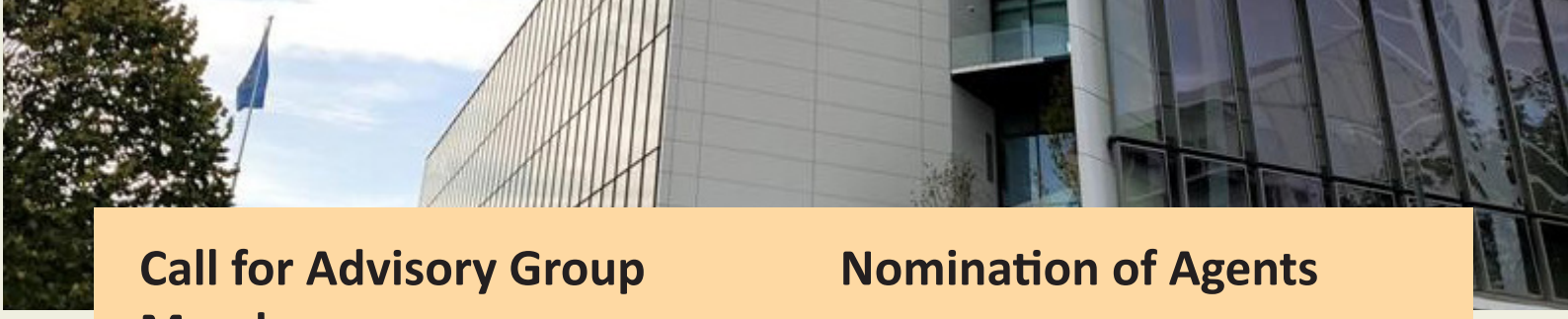
NK: I am the other half of the Production Team and, alongside Solene, make sure volumes go from first draft to publication.

HM: I am a technical editor. After a monograph has been rigorously checked by the scientists, I help to ensure accuracy and clarity and apply WHO house style.

If you were to recommend one place in Lyon to visit, where would it be and why?

NK: This is a difficult question as there is so much to pick from. I will choose Parc de la Tete d'Or. It is beautiful all year round, from the depths of winter to high summer. There is always something to enjoy – no matter your age.

HM: If you like hiking, Lyon is a great base. I particularly like the fact that Lyon is near the French Alps and you can see Mont Blanc (4800 m) on the horizon on a clear day.



Call for Advisory Group Members

Advisory Group Members prepare preliminary pre-meeting materials and participate in a 4-day meeting to recommend priorities for the *IARC Monographs* during 2025–2029.
Eligible scientists generally have published significant research related to carcinogenicity of environmental, behavioural, or occupational factors that can increase the risk of human cancer, or in exposure characterization for carcinogens. They may also have expertise in carcinogen testing and/or in carcinogen hazard evaluation. Consideration is also given to diversity in scientific approaches and views, as well as geographical representation. Self-nominations and nomination of women and of candidates from low- and middle-income countries are particularly encouraged.

For more information on the Advisory Group to Recommend Priorities for the *IARC Monographs*, please see the *IARC Monographs* website.

Nomination of Agents

For each new volume of the *IARC Monographs*, IARC selects the agents for review from those recommended by the most recent Advisory Group Report, considering the availability of pertinent research studies and current public health priorities. IARC encourages the general public, the scientific community, national health agencies, and other organizations to nominate agents for review in future *IARC Monographs* volumes.

If you would like to nominate an agent, please complete the online form (one agent per form) and the accompanying WHO Declaration of Interests. Please contact IARC at priorities@iarc.who.int for further information.

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Published in 2023

IARC Monographs

May 2023: Volume 131

Cobalt, antimony compounds, and weapons-grade tungsten alloy

Available from:
https://publications.iarc.fr/618

Anticipated by 31 July 2023: Volume 132

Occupational exposure as a firefighter

The Lancet Oncology

Cattley RC, Kromhout H, Sun M, et al. (2023). Carcinogenicity of anthracene, 2-bromopropane, butyl methacrylate, and dimethyl hydrogen phosphite. *The Lancet Oncology*. Published online 23 March 2023

Riboli E, Beland F, Lachenmeier D, et al. (2023). Carcinogenicity of aspartame, methyleugenol, and isoeugenol. *The Lancet Oncology*. Published online 14 July 2023

IARC
25 avenue Tony Garnier
CS 90627
69366 Lyon
CEDEX 07 France

Email: imonews@iarc.who.int
Web: https://monographs.iarc.who.int/