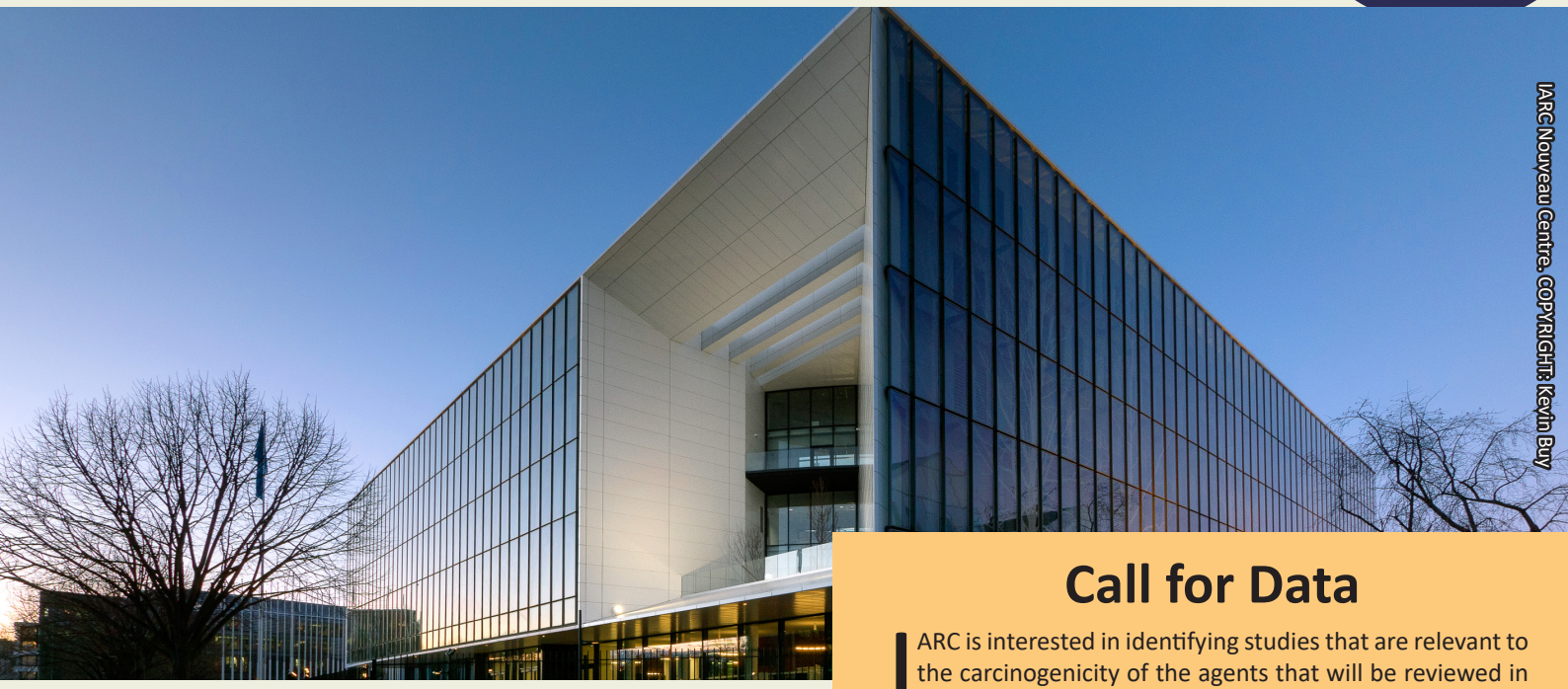
IARC MONOGRAPHS NEWS

A newsletter from the *IARC Monographs* programme

December 2024
Issue No. 10



IARC Nouveau Centre. COPYRIGHT: Kevin Buy

3rd anniversary of IMO News

This issue marks 3 years since the introduction of the *IARC Monographs* newsletter (IMO News) as part of our 50th anniversary celebrations. Issue No. 10 ushers in a change to one of our regular features: on p. 4, we highlight the experiences of early career scientists who have joined the most recent *IARC Monographs* meetings. We hope you enjoy experiencing the *Monographs* process through their fresh perspective.

In other news, we present the results of Meeting 137, the classification of three pharmaceuticals (hydrochlorothiazide, voriconazole, and tacrolimus) in Group 1 (see p. 2). We also announce several important new publications (see p. 5), including the complete Volume 134 on aspartame, methyleugenol, and isoeugenol; the latest report of our Advisory Group on Priorities; and a new volume in IARC's seminal Scientific Publication series, *Statistical Methods in Cancer Research*. On p. 3, our senior epidemiologist, Andrew Kunzmann, interviews the three co-editors of this new volume, which outlines approaches for the evaluation of biases in case–control and cohort studies used for cancer hazard identification. We invite you to join us for a webinar on 29 January 2025 to introduce this new volume to the scientific community.

We encourage you to write to us at imo@iarc.who.int with suggestions for features in future newsletters.

Mary Schubauer-Berigan

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 138: Automotive gasoline and some oxygenated additives

Meeting dates: 25 February to 4 March 2025
Call for Data closing date: 24 January 2025
Call for Experts CLOSED: 3 June 2024

Meeting 139: Hepatitis D virus, human cytomegalovirus, and Merkel cell polyomavirus

Meeting dates: 3–10 June 2025
Call for Data closing date: 1 May 2025
Call for Experts CLOSED: 15 August 2024

Meeting 140: Atrazine, alachlor, and vinclozolin

Meeting dates: 28 October to 4 November 2025
Call for Data closing date: 22 September 2025
Call for Experts closing date: 16 December 2024

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 137: Hydrochlorothiazide, voriconazole, and tacrolimus

Meeting held on 5–12 November 2024 in Lyon, France

A summary of the results of Meeting 137 has now been published in *The Lancet Oncology*.

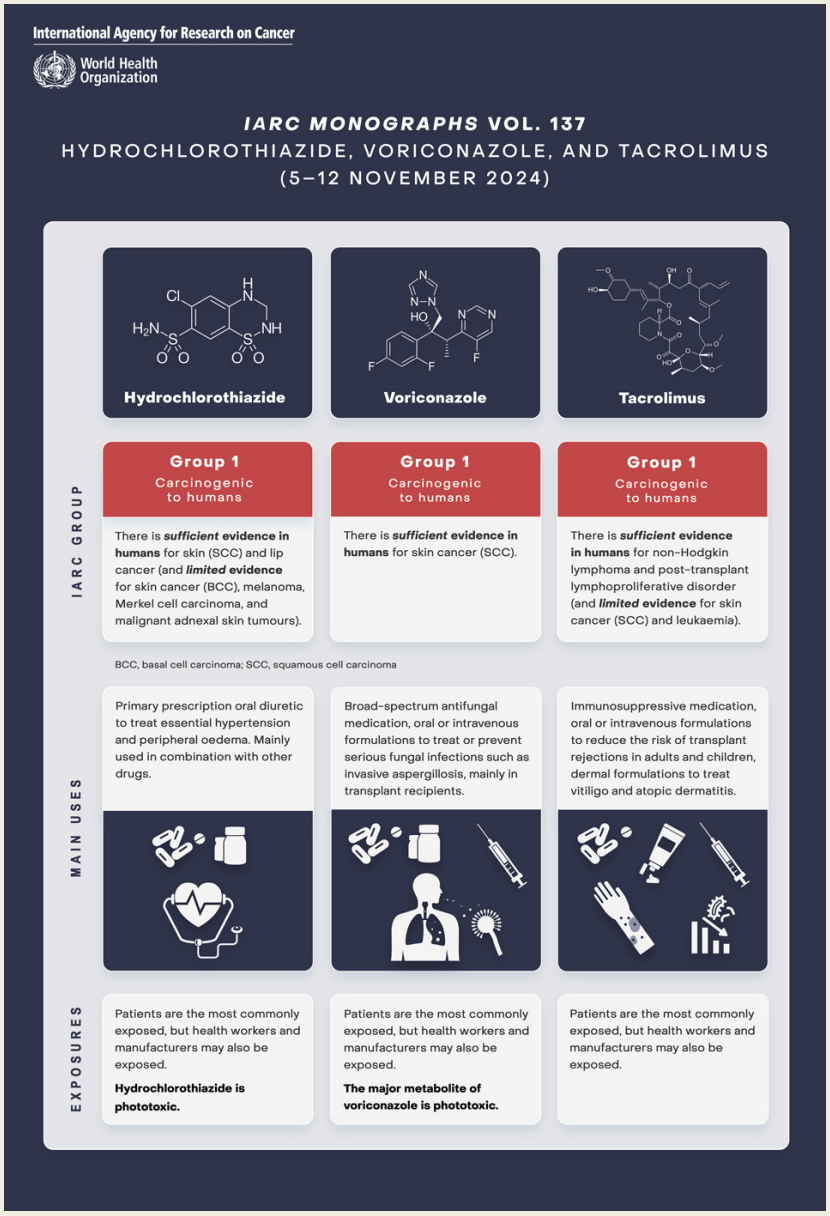
Hydrochlorothiazide is the most common prescription-only oral thiazide drug used worldwide to treat essential hypertension and peripheral oedema. Voriconazole is a broad-spectrum triazole drug used to cure or prevent invasive aspergillosis and other serious fungal infections, which are common in transplant recipients. Tacrolimus is a calcineurin inhibitor used orally and intravenously as an immunosuppressant to reduce the risk of rejection of solid organ transplants and prevent graft-versus-host disease, and topically to treat atopic dermatitis and vitiligo. All three drugs are listed as essential medicines by the World Health Organization.

The Working Group evaluated all three drugs as *carcinogenic to humans* (Group 1).

There was *sufficient* evidence that hydrochlorothiazide causes squamous cell carcinoma of skin and cancer of the lip in humans. The evidence was *limited* for basal cell carcinoma of skin, melanoma of the skin, Merkel cell carcinoma, and malignant adnexal skin tumours. There was *sufficient* evidence for cancer in animals and *limited* mechanistic evidence. Hydrochlorothiazide is phototoxic.

There was *sufficient* evidence that voriconazole causes squamous cell carcinoma of skin in humans. There was *strong* mechanistic evidence that voriconazole combined with ultraviolet radiation induces oxidative stress and precancerous lesions of the skin.

There was *sufficient* evidence that tacrolimus causes non-Hodgkin lymphoma and post-transplant lymphoproliferative disorder. The evidence was *limited* for leukaemia and squamous cell carcinoma of the skin in humans. There was also *sufficient* evidence for cancer in animals, and strong mechanistic evidence of immunosuppression.



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Bias Assessment in Case–Control and Cohort Studies for Hazard Identification

Statistical Methods in Cancer Research, Volume V

Volume editors: Amy Berrington de González, David B. Richardson, and Mary Schubauer-Berigan

What was the motivation for the book? What gap did you see that needed filling?

DBR: The challenges faced by Working Groups for the *IARC Monographs* originally motivated this book. Over the years, there has been a lot of creative thinking done by Working Groups to assess biases in studies. This book brings tools for assessing bias that may help Working Group members.

Who is the target audience and how do you think they will use the book?

ABdG: Primarily, cancer epidemiologists who are conducting reviews of the literature. But also, researchers who want to include sensitivity analyses of potential biases in the Results sections of their research articles. We hope that this will eventually replace the ubiquitous "laundry list" of biases in the Discussion section with a more nuanced evaluation of the probable direction and potential magnitude of each bias.

How might the book be used differently for hazard identification versus risk assessment?

ABdG: We want to remind researchers to think carefully about the difference between hazard identification and risk assessment, and then to evaluate the biases in that context. For hazard identification, if you have a positive study then you should focus on identifying biases away from the null. Correcting biases towards the null will not change your interpretation. For risk assessment, you have to think about biases in both directions.

MS-B: Although the main audience is those involved in cancer hazard identification, there are elements that lend themselves to consideration by risk assessors. For example, regression calibration and other methods to "de-bias" published risk estimates could be very useful in providing more accurate exposure–response coefficients for use in risk assessment.

Why did you decide to publish this as part of the IARC *Statistical Methods in Cancer Research* series?

MS-B: The aims, approach, and reach of the first two volumes in this series (fondly known as the "Breslow & Day" books) really resonated with the editors. We view Volume V as the natural successor to these seminal volumes and hope that it enjoys even a fraction of the utility and longevity that Volumes I and II have.

How would you explain this book's advice to non-epidemiologists?

MS-B: We cannot randomly assign people to have (or not have) long-term exposures to agents that could cause them serious harm many years into the future. For this reason, observational studies – in which we study people who do or do not have an exposure throughout the course of their lives – provide the best evidence we have about the direct health effects (e.g. cancer) of such exposures. Observational studies may have biases because of the lack of randomization, the quality of exposure and outcome measurement, and the way the participants are selected (by themselves or the investigators) for inclusion in the study. This book gives real-world examples of how to determine whether such biases are sufficiently important that they could change the conclusions about whether exposure to the agent can cause cancer or other long-term health problems.

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Why did you choose the four examples of bias that are included in the book?

ABdG: They are all examples from *IARC Monographs* reviews that illustrate the range of potential biases that Working Groups have had to evaluate. They also vary from agents for which there are many informative human studies (e.g. red meat) to those with relatively few (e.g. mobile phones). This enabled us to illustrate how you can incorporate bias assessment into evidence synthesis in these two very different scenarios.

DBR: The use of directed acyclic graphs (DAGs), for example, has not always been typical in the *IARC Monographs*, but served a useful role in the evaluation of opium, which was therefore taken as an example for that tool.

Interview by Andrew Kunzmann

Webinar on Scientific Publication No. 171
Find out more about the book from the lead authors
29 January 2025, 16:00–17:30 CET
Registration now open

REGISTER

Introducing three IARC Early Career Scientists

Julia Rezende Da Silva (ESC), Yue Zhai (NME), and Laia Peruchet (NME)

What did you enjoy most about Meeting 137?

JRdS: I truly enjoyed the opportunity to engage with scientists from around the world, each bringing unique perspectives. It was fascinating to learn from them and see how diverse scientific fields, such as toxicology and epidemiology, can come together to inform decision-making paradigms.

YZ: I enjoyed observing the scientific discussions in the subgroup, the peer-review process between subgroups, and the whole process of triangulating evidence. These are things that we rarely have the opportunity to see in our daily work.

From left to right: Xiaobei Deng, Laia Peruchet, Julia Rezende Da Silva, Yue Zhai, Azam Majidi, and Yahya Mahamat-Saleh, early career and visiting scientists who participated in Meeting 137.

LP: The long discussions between leading experts from all over the world and the extreme scientific rigour that guides these discussions.

Would you like to participate in another *IARC Monographs* meeting? If yes, why?

JRdS: Absolutely! I would be honoured to participate again and contribute to the process of identifying cancer hazards, as it can play a critical role in shaping public health policies.

YZ: Yes. Participating in this *Monographs* meeting helped me to put our own epidemiological research work into a bigger and more meaningful context. I would like to participate in another meeting to learn more from the experts and the IARC secretariat.

LP: I would be thrilled to participate again, given the significant impact of these reviews. Additionally, since the topics are not always within my primary research field, it would be highly enriching to gain a broader perspective on carcinogens.

Call for Experts

Working Group Members are responsible for all scientific reviews and evaluations developed during the *IARC Monographs* meeting. The Working Group is interdisciplinary and comprises subgroups of experts in the fields of: (1) exposure characterization; (2) cancer in humans; (3) cancer in experimental animals; and (4) mechanistic evidence.

IARC selects Working Group Members on the basis of expertise related to the subject matter and relevant methodologies, and absence of conflicts of interest. Consideration is also given to diversity in scientific approaches and views, as well as demographic composition. Self-nominations and nomination of women and of candidates from low- and middle-income countries are particularly encouraged.

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.

Published in 2024

IARC Monographs

Anthracene, 2-Bromopropane, Butyl Methacrylate, and Dimethyl Hydrogen Phosphite

June 2024: Volume 133

Available from:
https://publications.iarc.who.int/631

Aspartame, Methyleugenol, and Isoeugenol

September 2024: Volume 134

Available from:
https://publications.iarc.who.int/627

IARC Scientific Publication

Bias Assessment in Case–Control and Cohort Studies for Hazard Identification (Statistical Methods in Cancer Research, Volume V)

September 2024

Available from:
https://publications.iarc.who.int/634

IARC Advisory Group Report

Advisory Group recommendations on priorities for the *IARC Monographs* during 2025–2029

November 2024

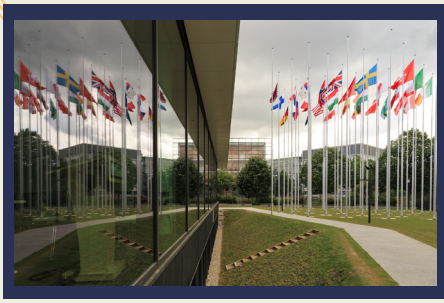
Report available online

The Lancet Oncology

Cogliano VJ, Corsini E, Fournier A, Nelson HH, Sergi CM, Antunes AMM, et al. (2024). Carcinogenicity of hydrochlorothiazide, voriconazole, and tacrolimus. *The Lancet Oncology*. Published online 29 November 2024

Stayner L, Carreón-Valencia T, Demers P, Fritz J, Sim M, Stewart P, et al. (2024). Carcinogenicity of talc and acrylonitrile. *The Lancet Oncology*. Published online 5 July 2024

Berrington de González A, Masten SA, Bhatti B, Fortner RT, Peters S, Santonen T, et al. (2024). Advisory Group recommendations on priorities for the *IARC Monographs*. *The Lancet Oncology*. Published online 12 April 2024



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