IARC MONOGRAPHS NEWS

A newsletter from the *IARC Monographs* programme

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Update on Filling Research Gaps: Progress Since 2009 Workshop

The *IARC Monographs* serve a dual role in cancer hazard identification: expert Working Groups synthesize the latest evidence to reach robust conclusions on carcinogenicity, thereby uncovering gaps in the available research.

The programme generally avoids making explicit research recommendations. However, in 2009, IARC convened a workshop in Lyon in collaboration with other organizations. The aim of the workshop was to systematically review gaps and identify research recommendations for 20 occupational agents with unresolved carcinogenicity. An update on progress made in filling these research gaps was recently published by *Monographs* scientists and collaborators. The major finding was that gaps had been filled, and classifications had advanced, for nearly half the agents. An accompanying perspective emphasized the value of the workshop in planning etiological research on occupational carcinogens.

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.

Advisory Group to Recommend Priorities for the *IARC Monographs* during 2025–2029
Meeting dates: 19–22 March 2024
Call for Nomination of Agents CLOSED: 30 November 2023
Call for Experts CLOSED: 31 July 2023

Meeting 136: Talc and Acrylonitrile
Meeting dates: 11–18 June 2024
Call for Data closing date: 10 May 2024
Call for Experts CLOSED: 31 July 2023

Meeting 137: Hydrochlorothiazide, Voriconazole, and Tacrolimus
Meeting dates: 5–12 November 2024
Call for Data closing date: 5 October 2024
Call for Experts closing date: 15 January 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

The Team

Introducing Lamia Benbrahim-Tallaa and Mathieu Rose.

Where are you originally from?

LT: I was born and raised in Algiers, Algeria. I left in 1994 and have since lived in the USA and France.

MR: I am from Paris and spent the last 15 years in London, UK.

How long have you been at IARC?

LT: I joined the *IARC Monographs* team 16 years ago, in September 2007.

MR: I joined the *IARC Monographs* team in April 2023.

What is your role in the IMO team?

LT: I am a toxicologist and serve as Lead Rapporteur for Section 3, Cancer in experimental animals. I also regularly act as Responsible Officer, overseeing the organization of a *Monographs* meeting.

MR: I am the Information Technology Database and Web Developer in charge of the maintenance and development of specialized and secure technology solutions for online systematic reviews, developing the *IARC Monographs* Online Database, and providing technological support to our team.

If you were to recommend one place in Lyon to visit, where would it be and why?
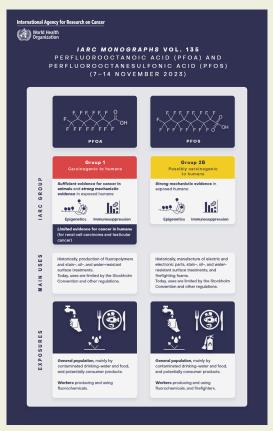
LT: I would like to recommend the medieval village of Pérouges, around 30 km from Lyon, and one of the most beautiful villages in France. Its superbly preserved architecture, straight out of the Middle Ages, takes you back in time.

MR: Not far from the IARC agency, you will find the Musée des Confluences. At the confluence of the rivers Rhône and Saône, it is one of the most popular museums in Lyon and definitely the one with the most unique architecture.

Results of *IARC Monographs* Meeting 135: Perfluorooctanoic acid (PFOA) and Perfluorooctanesulfonic acid (PFOS)

Meeting held in Lyon between 7–14 November 2023

Click to enlarge

PFOA and PFOS are per- and polyfluoroalkyl substances (PFAS) that are extremely resistant to degradation. PFOA and PFOS have been used in a wide range of applications, such as production of fluoropolymers; aerosol propellants; solvents; pesticides; antifoaming agents; surface treatments for household products, textiles, leather, masonry, and paper and board including food packaging; levelling agents in paints, coatings, and waxes; plastics; lubricants and greases; and in firefighting foams.

Both PFOA and PFOS are listed in the Stockholm Convention on Persistent Organic Pollutants, but exposure persists via continued use in some countries and legacy contamination. Although occupationally exposed populations have some of the highest levels of exposure, there are high levels at pollution sources, and PFOA and PFOS occur ubiquitously in the environment.

The Working Group evaluated PFOA as *carcinogenic to humans* (Group 1) on the basis of *sufficient* evidence for cancer in experimental animals and *strong* mechanistic evidence that PFOA exhibits key characteristics of carcinogens in exposed humans. There was *limited* evidence in humans for cancer of the testis and for renal cell carcinoma. PFOS was evaluated as *possibly carcinogenic to humans* (Group 2B) on the basis of *strong* mechanistic evidence. There was *limited* evidence for cancer in experimental animals and *inadequate* evidence for cancer in humans.

A summary of the results of *IARC Monographs* Meeting 135 has now been published in *The Lancet Oncology*.

IARC Monographs Scientific Workshop on Key Characteristics-associated End-points for Evaluating Mechanistic Evidence of Carcinogenic Hazards

Information on mechanisms induced by carcinogenic exposures has been considered for the overall evaluation of carcinogenic hazard since early *IARC Monographs* volumes. Initially, such mechanistic evidence was mainly used to determine whether the overall evaluation, which was based on evidence of cancer in humans and cancer in experimental animals, should be modified in view of the strength of the mechanistic evidence. Subsequent advances in tools and technology have allowed decades of discovery and the development of a deep understanding of the mechanisms underlying carcinogenesis. At the same time, the heterogeneity and volume of the mechanistic data are challenges when identifying and organizing the relevant evidence associated with a specific exposure.

Participants and IARC Secretariat at the 2023 Key Characteristics Workshop

The implementation of the "10 key characteristics of carcinogens" framework [1, 2] has significantly improved the way in which mechanistic evidence is evaluated in the *IARC Monographs*. The prominence of mechanistic evidence was finally recognized formally in the most recent update to the Preamble to the *IARC Monographs* in 2019 [3].

Since its introduction, the key characteristics of carcinogens (KCs) framework has been applied to 99 agents evaluated in 23 volumes of the *IARC Monographs*. This framework has brought uniformity to *IARC Monographs* assessments and allowed a focused systematic review of the publicly available literature on mechanisms of carcinogens. Importantly, it has contributed to advancing the science by which mechanistic evidence is used to evaluate potential carcinogens. Thus, it was considered timely to review aspects of how the KCs have been applied in past years, especially after the update to the Preamble, and to discuss suggested improvements to the process.

On 23–28 July 2023, 29 scientists from 8 countries met with IARC scientists in Lyon to discuss: (i) interpretation of end-points forming the evidence base for the KCs; (ii) incorporation of data from emerging assays and biomarkers into the KCs; and (iii) integration of mechanistic evidence as part of cancer hazard identification. The workshop material will result in the publication of an IARC Technical Report and one or more accompanying peer-reviewed manuscripts that will support future Working Groups of experts in the reporting and interpretation of results under the KCs framework of mechanistic evidence evaluation within the *IARC Monographs* or in other contexts. The publication of the IARC Technical Report is expected in early 2024.

Aline de Conti, Caterina Facchin, and Federica Madia

References:

1 Smith MT, Guyton KZ, Gibbons CF, Fritz JM, Portier CJ, Rusyn I, et al. (2016). Key characteristics of carcinogens as a basis for organizing data on mechanisms of carcinogenesis. *Environ Health Perspect*. 124(6):713–21. Available from: http://dx.doi.org/10.1289/ehp.1509912.

2 Smith MT, Guyton KZ, Kleinstreuer N, Borrel A, Cardenas A, Chiu WA, et al. (2020). The key characteristics of carcinogens: relationship to the hallmarks of cancer, relevant biomarkers, and assays to measure them. *Cancer Epidemiol Biomarkers Prev*. Available from: https://doi.org/10.1158/1055-9965.epi-19-1346.

3 IARC (2019). Preamble to the IARC Monographs (amended January 2019). Lyon, France: International Agency for Research on Cancer. Available from: https://monographs.iarc.who.int/iarc-monographs-preamble-preamble-to-the-iarc-monographs/.

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.

While the formal call for nominations has closed for consideration by the 2024 Advisory Group, urgent public health priorities can be considered at any time.

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.

Published in 2023

IARC Monographs

May 2023: Volume 131

Cobalt, antimony compounds, and weapons-grade tungsten alloy

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

July 2023: Volume 132

Occupational exposure as a firefighter

Available from:
https://publications.iarc.fr/615

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

Zahm S, Bonde JP, Chiu WA, et al. (2023). Carcinogenicity of perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS). *The Lancet Oncology*. Published online 30 November 2023