IARC MONOGRAPHS NEWS

A newsletter from the *IARC Monographs* programme

March 2025 Issue No. 11

Highlights from Spring 2025

Spring 2025 finds us abounding in new growth here in Lyon. It has been an active period for us in the *IARC Monographs* programme, as you can see by perusing this issue of the newsletter. On this page, you will find the calls for data and experts for newly announced Meeting 141 on three chemicals: tris(chloropropyl)phosphate (a flame retardant), cumyl hydroperoxide, and butyraldehyde. All three agents were accorded high priority for evaluation by our *Advisory Group to Recommend Priorities for the* IARC Monographs *during 2025–2029*; none have been previously evaluated in the *Monographs* programme.

On p. 2, we present the results of Meeting 138, which classified automotive gasoline in Group 1 and five oxygenated gasoline additives in Groups 2B or 3. We highlight the perspectives of early career scientists who joined Meeting 138 on p.4.

On p.3, our senior toxicologist, Federica Madia, interviews the Chair on the major outcomes of a Scientific Workshop convened by IARC on the furtherance of the key characteristics of carcinogens for cancer hazard identification.

We also announce the much-anticipated publication (see p.5), of Volume 135 on perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS).

As always, your suggestions for features in future newsletters are welcomed at imo@iarc.who.int.

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

Meeting dates: 3 to 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 CLOSED: 16 December 2024

Meeting 141: Tris(chloropropyl)phosphate, butyraldehyde, and cumyl hydroperoxide

Meeting dates: 3–10 March 2026
Call for Data closing date: 2 February 2026
Call for Experts closing date: 2 June 2025

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 138: Automotive gasoline and some oxygenated gasoline additives

Meeting held on 25 February to 4 March 2025 in Lyon, France

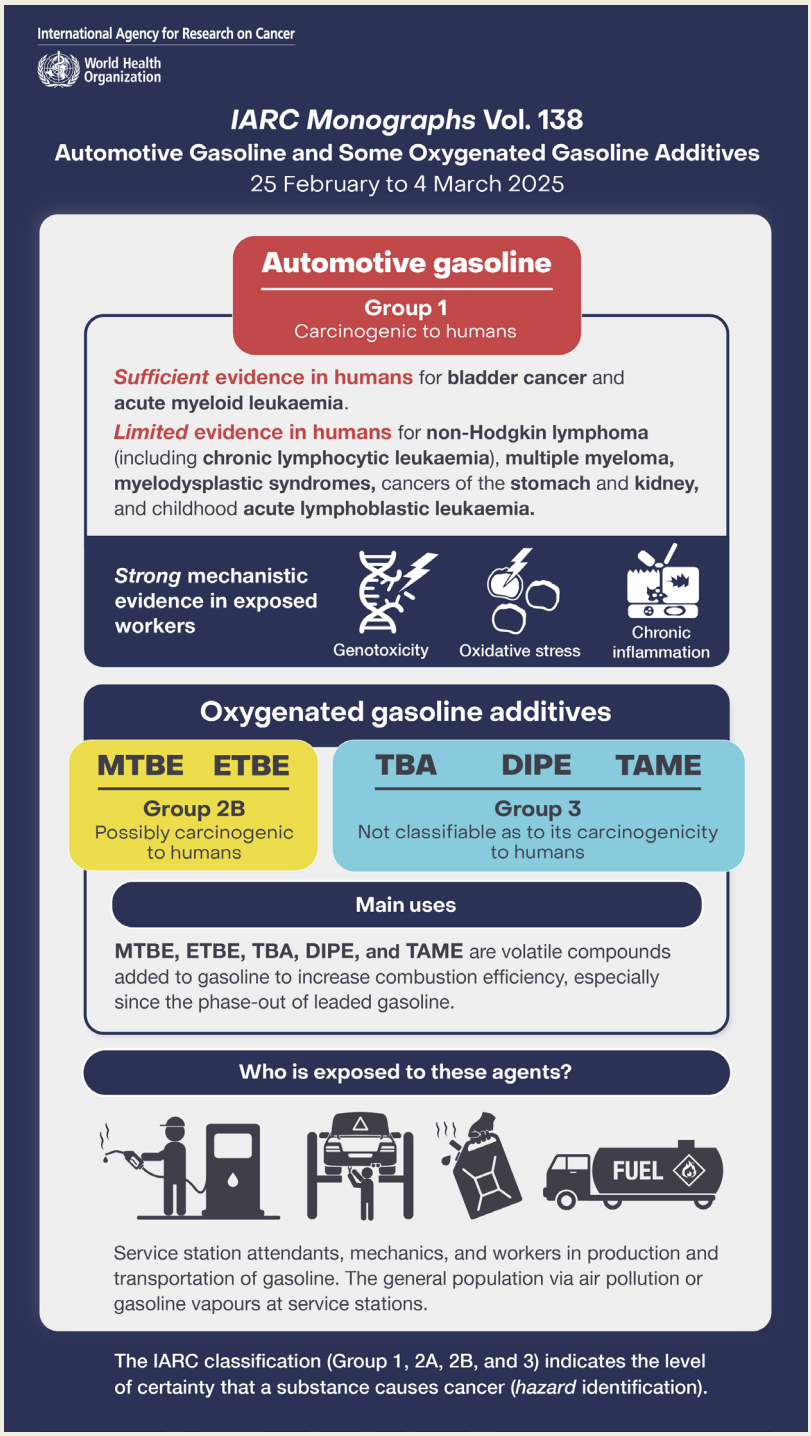
A summary of the results of Meeting 138 has now been published in *The Lancet Oncology*.

Automotive gasoline, methyl *tert*-butyl ether (MTBE), ethyl *tert*-butyl ether (ETBE), *tert*-butyl alcohol (TBA), diisopropyl ether (DIPE), and *tert*-amyl methyl ether (TAME) were accorded high priority by the *Advisory Group to Recommend Priorities for the* IARC Monographs *during 2020–2024*.

Automotive gasoline, a commercial product, is a complex mixture used as a fuel in internal combustion engines. The typical components are volatile, petroleum-derived hydrocarbons. MTBE, ETBE, TBA, TAME, and DIPE are volatile oxygenated additives used in gasoline to increase combustion efficiency.

The Working Group evaluated automotive gasoline as *carcinogenic to humans* (Group 1) on the basis of *sufficient* evidence for cancer in humans, and the combination of *sufficient* evidence for cancer in experimental animals and *strong* mechanistic evidence in exposed humans. Automotive gasoline causes cancer of the urinary bladder and acute myeloid leukaemia in adults. The evidence was *limited* for childhood acute lymphoblastic leukaemia, and for non-Hodgkin lymphoma (including chronic lymphocytic leukaemia), multiple myeloma, myelodysplastic syndromes, and cancers of the stomach and kidney.

MTBE and ETBE were both classified as *possibly carcinogenic to humans* (Group 2B) on the basis of *sufficient* evidence for cancer in experimental animals and (for ETBE) *strong* mechanistic evidence. TBA, DIPE, and TAME were each evaluated as *not classifiable as to its carcinogenicity to humans* (Group 3). For all the oxygenated additives, the evidence regarding cancer in humans was *inadequate.*



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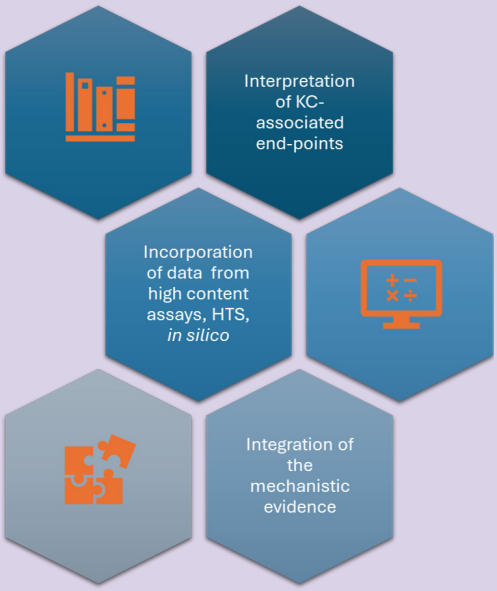
An interview with Dr David DeMarini on the recent commentary on the IARC Workshop on the Key Characteristics of Carcinogens

A Commentary on the IARC Scientific Workshop on *Key Characteristics-associated End-points for Evaluating Mechanistic Evidence of Carcinogenic Hazards* was recently published in the February issue of *Environmental Health Perspectives*.[1] We asked Dr David DeMarini, who chaired the workshop, for a few highlights from the discussions.

FM: What was the motivation for the IARC scientific workshop? And what main themes were discussed?

DD: The key characteristics (KCs) of carcinogens[2,3] had been used by Working Groups of *IARC Monographs* for approximately 10 years by the time this workshop was held.[2,4] The IARC Secretariat recognized the value of evaluating the experience in the application of the KCs and clarifying both the relevance of some of the KCs-associated end-points and the KC to which a particular end-point or assay result should be assigned. In addition, newer types of data[5] that were less common when the KCs were first created have become available for recent *Monographs* but do not fit neatly into the KCs framework. Therefore, in July 2023, IARC convened in Lyon a Scientific Workshop of international experts across different disciplines to discuss these topics. The main themes upon which the workshop focused included: (a) an appraisal of the use of the KCs during the previous 10 years, identifying areas for improvement in the interpretation of the end-points; (b) ways to incorporate data from high-content and high-throughput assays into the KCs, especially transcriptomic and metabolomic data; (c) case studies on how mutational signatures can be informative and subsequently incorporated into the KCs; (d) criteria for inclusion of in silico data; (e) approaches to integrate mechanistic evidence as part of cancer hazard identification; (f) discussion on the KCs relative to other mechanistic-type approaches to hazard identification; and (g) ways to incorporate artificial intelligence (AI) tools into systematic literature review.



FM: The Commentary refers to almost 100 agents being evaluated with the KCs. What are the major insights gained from this experience for the *IARC Monographs* programme and for the invited experts?

DD: The workshop participants found that, among the agents evaluated thus far under the KCs framework, agents exhibit three KCs (on average) with consistent and coherent evidence. KC 2 (genotoxicity) is the most commonly exhibited KC. Over the years, in the *Monographs* there has also been an increase in the volume of data informing KCs 4, 5, 7, and 8 across all test systems. The majority of the consistent and coherent evidence for KC 4 (epigenetic alterations) has been observed in studies in exposed humans. In contrast, no agent has exhibited KC 9 (causes immortalization). Omics data, especially transcriptomics, are clearly important end-points associated with KC 4 and other KCs, and criteria were developed to identify the most informative studies. In addition, workshop participants identified the need for both new high-throughput assays that more clearly align with the KCs, and cancer in general, and for ways to improve their inclusion and evaluation. The experts also discussed opportunities to apply AI to enhance the organization and use of such data for the *Monographs*.

FM: How will discussions on the interpretation of the KC-associated end-points be relevant for future *Monographs* evaluations?

DD: The Technical Report of the Workshop (in prepara-

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tion) will describe nuanced approaches to the interpretation of the various end-points that should be helpful to future Working Groups and that should reduce ambiguity when attempting to categorize data into the KCs framework. Furthermore, the workshop attendees proposed a series of efforts that, once implemented, will improve the application of the KCs and make the assessment process easier and less burdensome for the Working Group, ensuring consistency and uniformity across different evaluations.

Federica Madia

From left to right: Federica Madia, Mathieu Rose, David DeMarini, Aline de Conti, and Mary Schubauer-Berigan.

Five IARC Early Career and Visiting Scientists contributing to Meeting 138

Abdoulaye Barry (ENV), Rachmad Anres Dongoran (EGM), Roya Dolatkhah (ENV), Esther Gonzales-Gil (NME), and Felix Onyije (ENV)

Where are you originally from and how long have you been at IARC?

AB: I am originally from Guinea and have been at IARC for a total of 5 months.

RAD: I am from Indonesia and am in my first year at IARC.

RD: I am from Iran and have had the pleasure to be at IARC since early 2023.

EG: I am originally from Huesca in Spain. I started work at IARC in March 2022, so 3 years already.

FO: I am originally from Nigeria and have been at IARC for 5 years.

From left to right: Rachmad Anres Dongoran, Abdoulaye Barry, Esther Gonzalez Gil, Roya Dolatkhah, and Felix Onyije, Early Career and Visiting Scientists (ECVS) who participated in Meeting 138.

What is your usual role in your group at IARC?

RAD: I am a Postdoctoral Fellow in the EGM Branch, conducting research on oral cancer. My current project focuses on profiling microbiomes, genomics, and epigenetics, including in patients with oral cancer who have no identified risk factors.

RD: I am currently working as a Visiting Scientist in the ENV Branch, focusing on the Childhood Cancer and Leukemia International Consortium (CCLIC) Data Coordination Center. I am also conducting research on childhood cancer, examining the association between environmental exposures, lifestyle factors, and the risk of childhood cancer.

What did you enjoy most about the *Monographs* meeting?

AB: I really enjoyed the engaging discussions with experts and learning about the classification process. Additionally, the *Monographs* meeting helped me refine my attention to detail, precision, and teamwork skills.

EG: It was great to be present in the discussions and to witness all the process. Everything was very well organized. I feel this is something that all ECVSs should experience before leaving IARC.

FO: What I enjoyed most in my subgroup was the in-depth scrutiny of the various studies that formed the bases of the evaluation outcomes. I enjoyed the level of thoroughness on the part of the experts, the rigour and critique involved before reaching a conclusion. On the part of the Secretariat, excellent organization, and timely availability of materials for the Working Group.

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 2025

IARC Monographs

Perfluorooctanoic Acid (PFOA) and Perfluorooctanesulfonic Acid (PFOS)

February 2025: Volume 135

Available from:
https://publications.iarc.who.int/636

The Lancet Oncology

Turner MC, Godderis L, Guénel P, Hopf N, Quintanilla-Vega B, Coelho Soares-Lima SC, et al. (2025). Carcinogenicity of automotive gasoline and some oxygenated gasoline additives. *The Lancet Oncology*. Published online 21 March 2025

Commentary

DeMarini DM, Gwinn W, Watkins E, Reisfeld B, Chiu WA, Zeise L, et al. (2025). IARC Workshop on the key characteristics of carcinogens: assessment of end points for evaluating mechanistic evidence of carcinogenic hazards. *Environmental Health Perspectives*. 133(2):25001. https://ehp.niehs.nih.gov/doi/10.1289/EHP15389

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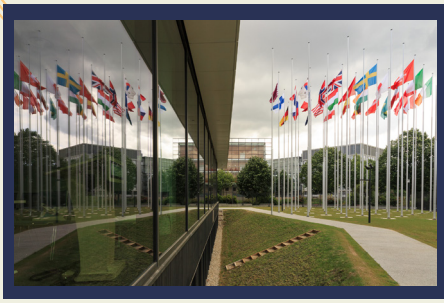

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