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Engaging With International Carcinogen Evaluations

By **Eric Lasker and John Kalas** (November 14, 2019, 4:55 PM EST)

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This July, the International Agency for Research on Cancer, or IARC, released its 2020-2024 priority list for evaluation.[1] Defense-oriented attorneys and corporations should be aware of the list and begin preparing for eventual evaluations by IARC working groups.

What Is IARC?

IARC is a branch of the World Health Organization located in Lyon, France. Tasked by the WHO with evaluating potential causes of cancer, IARC conducts hazard evaluations of suspected carcinogens two to three times a year.

The results of these evaluations are published in IARC monographs — summary publications that discuss the existing literature, and then apply a cancer classification based upon the Monograph Working Group evaluation. Under current IARC guidelines, it is impossible to classify any evaluated substance as "not carcinogenic" — the best the guidelines allow is "insufficient evidence to deem carcinogenic."[2]

Additionally, IARC monograph working groups — with few exceptions — are only allowed to review published data in the peer-reviewed literature regarding substances they review. In the case of regulated substances, where many safety studies are submitted to regulators, but are not placed in the peer-reviewed literature, this can create a situation where IARC working groups only review a subset of the available data on a given compound, potentially leading to erroneous conclusions based on incomplete data sets.

IARC evaluations have been at issue in litigation for decades, going back to the asbestos wars of the 1980s and 1990s. In recent years, IARC evaluations of the active ingredient in the pesticide Roundup — glyphosate — and the active ingredient in the drug Actos — pioglitazone — have spurred personal injury litigation surrounding the compounds.

An IARC classification of "carcinogenic" or "probably carcinogenic" results in automatic listing as carcinogenic under California's Proposition 65. Under Proposition 65, bounties are available to private citizens or organizations who bring lawsuits claiming products contain levels of listed carcinogens that exceed the state's safe harbor level. These Proposition 65 lawsuits have been brought alleging undisclosed carcinogens in products like coffee and French fries.[3]

The importance of IARC classifications to the plaintiffs bar has increased over the years, and in the case of Actos, a plaintiffs' tort attorney involved in Actos litigation was actually listed on the attendance list of an IARC working group meeting.[4] Courts in recent personal injury litigation have found that an IARC classification in and of itself is not definitive proof of general causation,[5] but the same court has also held that IARC's conclusions regarding specific areas of the science may be relied upon by experts in meeting the general causation burden.[6]

The 2020-2024 Priority List

IARC's priority list for 2020–2024 lists dozens of chemicals, pharmaceuticals and other exposures slated for IARC working group review over the next five years. In order to be placed on the IARC priority list, a substance must be nominated for review by IARC. Then, the advisory group for the priority list reviews the nominations and chemicals in question, and suggests priorities for review over the coming years. Members of the advisory group included both academic and governmental scientists.[7]

The Advisory Group recommended dozens of substances for review. Some of the more notable substances nominated for review between 2020–2024 include:

- Domestic talc products (previously classified as "possibly carcinogenic");
- Aspartame (not previously evaluated);
- Acrylamide (previously classified as "probably carcinogenic");
- PFOA (previously classified as "possibly carcinogenic");
- Radiofrequency electromagnetic fields (previously classified as "possibly carcinogenic");
- Cannabis (not previously classified);
- E-cigarettes (not previously classified);
- Metalworking fluids (not previously classified);
- Fertility treatments (not previously classified);
- Carbon nanotubes (previously classified as "possibly carcinogenic"); and
- Oxygenated gasoline additives (not previously classified).[8]

Many of these substances or exposures have been the subject of previous personal injury or Proposition 65 litigation,[9] but an upgrade in classification may spur additional litigation. Indeed, plaintiffs firms are already advertising for lawsuits regarding some of these exposures.[10] It also could create major headaches for cellular phone companies as they attempt to roll out 5G technology.

Unfortunately, IARC's conflict-of-interest policy has been applied inconsistently to the makeup of their working groups in the past. For instance, IARC excluded Andres Ahlbom, a scientist at the Karolinska Institute in Sweden, from the previous working group that evaluated radiofrequency electronmagnetic fields just prior to that group's meeting. The exclusion was based upon Ahlbom's work on the board of his brother's consulting company. The company had previously lobbied on behalf of companies regarding telecom issues.

According to IARC, Ahlbom's membership on the board created a perceived conflict of interest.[11] However, IARC allowed Dr. Lennart Hardell, another Swedish scientist, to participate in the evaluation of radiofrequency electronmagnetic fields, despite the fact that he had previously participated as a paid expert witness in litigation regarding alleged injuries from radiofrequency electromagnetic fields.[12]

Given IARC's disparate treatment of conflicts of interest in the past, it is possible that future working groups will lack a balance of viewpoints as well, leading to classifications

that do not reflect scientific consensus.[13]

How to Prepare for a Monograph Review

Companies, trade groups and other interested parties can prepare for IARC monograph reviews in a few ways.

Monitor Makeup of IARC Working Groups

First, closely monitor the makeup of IARC working groups. A preliminary list of participants is usually released in the months prior to the working group meeting. A review of the publications of those participants may give a sense of where the working group is likely to come out on their classification.

Doing this sort of advance scouting prior to the meeting may allow for greater preparation to respond when IARC does eventually release their classification.

Placing Data in Peer-Reviewed Literature

Second, consider what data may be placed in the peer-reviewed literature without negatively affecting business operations. The more data that can be placed in the literature, the more data IARC — under its guidelines — will be able to consider in its review. Greater availability of data may help scientists at IARC avoid mistakes in classification.

Send Observers to Working Group

Third, send observer(s) to the working group meeting in Lyon, France. Though individuals with IARC-designated conflicts of interest (i.e. consulting with industry) may not participate in working groups, they may observe much of the meeting.

Sending observers may help interested parties gain valuable insight into the thought process of the working group and the evidence they found most compelling to their ultimate classification.

Educate the Public and Regulators

Fourth, start educating the public and relevant regulatory and political bodies what goes into an IARC classification. Specifically, the public and relevant bodies should be aware that IARC often relies upon an incomplete data set, as the policies under which working groups operate do not allow for the review of data not in the peer-reviewed literature or publicly released by regulatory agencies.

Thus, in many cases, IARC working groups rely upon an incomplete data set that does not contain many of the regulatory guideline studies necessary for product registration in the U.S. and elsewhere. Additionally, the public and relevant bodies should be informed that an IARC evaluation is a hazard assessment — in other words, it's a determination that a substance might be carcinogenic at some dose, but it does not address whether the dose people are exposed to in their daily lives could cause cancer.

Prepare for Litigation

Finally, prepare for litigation — of both the Proposition 65 and personal injury varieties. Involve in-house and potentially outside counsel in developing a strategy to deal with regulatory fallout, in addition to potential litigation and customer concerns about a change in classification. During this preparation, be aware that many of the efforts outlined in the four points above may become subject to discovery.

By virtue of its association with the United Nations, and by the participation of many individuals associated with impressive institutions, IARC working group classifications may be held in high regard by jurors and/or members of the general public. It takes a concerted, coordinated effort to put an IARC classification in proper context. Industries associated with substances on the priority list for 2020–2024 should begin their preparations now.

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[1] See Advisory Group Recommendations on Priorities for the IARC Monographs, The Lancet Oncology (April 2019), https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(19)30246-3/fulltext.

[2] See IARC Update Frustrates Industry and NGOs, Chemical Watch (May 2, 2019) (discussing removal of "probably not carcinogenic to humans" classification from IARC preamble). https://chemicalwatch.com/77053/iarc-update-frustrates-industry-and-ngos.

[3] See The Secretive Non-Profit Gaming California's Health Laws, The Outline (June 18, 2018) (discussing Proposition 65 lawsuits), https://theoutline.com/post/4963/council-education-research-toxics-california-coffee-lawsuit-cancer-label?zd=1&zi=3qomg3uf.

[4] https://monographs.iarc.fr/wp-content/uploads/2018/06/mono108.pdf.

[5] See In Re Roundup Prods. Liab. Litig., ECF No. 45 at 12 ("[E]xpert opinions that simply parrot IARC's analysis and conclusions are somewhat off topic and are unduly limited, rendering them insufficient to satisfy the plaintiffs' burden at the general causation phase. A 'hazard assessment,' as IARC and other public health bodies define that inquiry, is not what the jury needs to conduct when deciding whether glyphosate actually causes NHL in people at past or current exposure levels. An expert who recites IARC's conclusions and analysis therefore may be offering a sound scientific opinion, but not an opinion that speaks squarely to the issue the jury must decide.").

[6] Id. at 30–31 (stating IARC's conclusions regarding animal bioassay data is relevant to the general causation inquiry).

[7] https://monographs.iarc.fr/wp-content/uploads/2019/02/AGP-ListofParticipants.pdf.

[8] The full priority list can be found here: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(19)30246-3/fulltext.

[9] See, e.g., Newman v. Motorola, 78 F. App'x 292 (4th Cir. 2003) (personal injury case for brain cancer from electromagnetic litigation).

[10] See Cell Phone Litigation, Lundy Lundy Soileau & South, https://lundylawllp.com/services/cell-phone-litigation/.

[11] See https://www.reuters.com/article/us-health-who-iarc-special-report-idUSKCN0XF0RF.

[12] Newman, 78 F. App'x at 293-94.

[13] See EPA Reaffirms Finding that Glyphosate Does Not Cause Cancer, USA Today (April 30, 2019) (EPA spokesperson describes IARC evaluation as "an outlier" as "it's the only agency globally that has connected glyphosate to cancer"), https://www.desmoinesregister.com/story/money/agriculture/2019/04/30/epa-glyphosate-does-not-cause-cancer-herbicide-weed-killer-carcinogens-monsanto-roundup-bayer-iowa/3624978002/.
