Testimony at the Subcommittee on Investigations & Oversight and Subcommittee on Environment Hearing – EPA's IRIS Program: Reviewing its Progress and Roadblocks Ahead

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Thank you for the opportunity to speak today. I am Dr. Julie Goodman, an epidemiologist and board-certified toxicologist at Gradient, an environmental sciences consulting firm. We assist public and private organizations in evaluating the risks of chemicals and other substances on human health and the environment. I have been developing and applying weight-of-evidence and systematic review methodology in a variety of settings for over 10 years. I taught a graduate-level class on this topic at Harvard University, and much of my work has been published in the peer-reviewed literature. I am presenting testimony today as an independent scientist. While my travel costs have been paid by my company, I am here today on my own time, and I am not being compensated for the time I spent preparing this testimony.

In 2011, a National Academy of Sciences (NAS) National Research Council (NRC) committee provided recommendations for the US Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS) Program in the context of a review of the formaldehyde assessment (NRC, 2011). In response, EPA released a Draft Handbook for IRIS Assessments in 2013 (US EPA, 2013). In 2014 and 2018, NAS reviewed and evaluated the IRIS assessment process more generally, including progress made since 2011 (NRC, 2014; NAS, 2018).

Both the 2011 and 2014 NAS reviews stated that the IRIS program lacked a clear conceptual framework and clear and transparent methods. Further, NAS concluded that EPA did not fully assess the weight of evidence or justify the selection of studies for the derivation of toxicity values. The 2014 NAS review also specifically called for the finalization of the draft IRIS Handbook. Since this time, EPA has made substantial improvements to the IRIS process, including the development and application of systematic review methods for evidence identification, evaluation, and integration, but not all of the identified issues have been resolved (NAS, 2018).

To date, EPA has shown progress on a chemical-by-chemical basis, using the IRIS Assessment Plans (IAPs) for uranium and ammonia (US EPA, 2018a,b) and Systematic Review Protocols for the IRIS chloroform and chromium assessments (US EPA, 2018c, 2019) as examples of its new portfolio approach. EPA announced it will move forward with a revised IRIS Handbook, which will be put through peer review and public comment processes this year. This is undoubtedly needed and a critically important step forward, and EPA is to be commended for these actions.

I note that while it is true that a "one-size-fits-all" protocol for all chemicals is not feasible, and details of the individual chemical assessments will vary based on the specific research questions identified and on the available data, all IRIS assessments will benefit from a clearly written framework that serves as a standard operating procedure (SOP) for agency systematic reviews. This SOP can be expanded to include chemical-specific tailoring, as needed, to each phase of specific chemical reviews. An iterative approach can be used to incorporate new issues and knowledge into the SOP as it becomes available.

To follow through on its intention to use systematic review and weight-of-evidence methodology for hazard identification, EPA needs to complete an individual assessment using the new process. My experience with developing these types of approaches has shown that it is important to apply a framework in a chemical-specific setting to determine where its strengths lie and where it falls short and should be revised.

IRIS assessments both identify hazards associated with chemicals and characterize these hazards by generating toxicity values. With regard to the latter, EPA is always limited to studies with sufficient data for dose-response analysis, so the Handbook should describe what will be done if these studies are not reflective of the science as a whole. In addition to studies that identify toxic effects, part of the hazard identification process is to consider studies that inform the mechanism of toxicity. EPA should indicate how it will consider this mechanistic evidence when deriving toxicity values. For example, if mechanistic studies clearly show a threshold effect, then it should be incorporated into the dose-response analysis, and linear low-dose extrapolation should not be applied.

There is no doubt that conducting systematic reviews takes more time and resources than non-systematic reviews. However, a completed Handbook (that can and should be revised to reflect the best available science) will go a long way towards expediting assessments and increasing transparency and consistency across assessments. More importantly, with an established standard procedure in place, EPA staff will have better guidance to conduct IRIS assessments in a systematic and unbiased manner. This will allow stakeholders and members of the public to better understand the process and provide input and, ultimately, will increase their confidence in EPA's assessments.

In conclusion, to address the NAS recommendations for the IRIS Program dating back to 2011, EPA needs to complete a general guidance framework for IRIS assessments in a revised Handbook. EPA also needs to complete assessments that both apply this guidance and demonstrate that dose-response analyses and toxicity value derivations will be informed by the overall weight of evidence and biological mechanisms.

References

National Academy of Sciences (NAS). 2018. "Progress Toward Transforming the Integrated Risk Information System (IRIS) Program: A 2018 Evaluation." Engineering, and Medicine, National Academies Press (Washington, DC), 129p. Accessed at http://nap.edu/25086.

National Research Council (NRC). 2011. "Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde." National Academies Press (Washington, DC). 194p., April. Accessed at http://www.nap.edu/catalog/13142.html.

National Research Council (NRC). 2014. "Review of EPA's Integrated Risk Information System (IRIS) Process." National Academies Press (Washington, DC), 204p. Accessed at http://www.nap.edu/catalog.php?record_id=18764.

US EPA. 2013. "Materials Submitted to the National Research Council Part I: Status of Implementation of Recommendations." Integrated Risk Information System Program. Submitted to National Research Council, 142p., January 30.

US EPA. 2018a. "IRIS Assessment Plan for Uranium (Oral Reference Dose) (Scoping and Problem Formulation Materials) [CASRN 7440-61-1] (Public Comment Draft)." National Center for Environmental Assessment (NCEA), EPA/635/R-17/787. 16p., January. Accessed at https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=338655.

US EPA. 2018b. "IRIS Assessment Plan for Ammonia and Ammonium Salts: Noncancer Assessment for Oral Exposure (Scoping and Problem Formulation Materials) [CASRN 7664-41-7] (Problem Formation Draft)." National Center for Environmental Assessment (NCEA), EPA/635/R-18/041. 32p., April. Accessed at https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=340338.

US EPA. 2018c. "Systematic Review Protocol for the IRIS Chloroform Assessment (Inhalation) [CASRN 67-66-3] (Preliminary Materials Draft)." EPA/635/R-17/486. 76p., January. Accessed at https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=338653.

US EPA. 2019. "Systematic Review Protocol for the Hexavalent Chromium IRIS Assessment (Preliminary Assessment Materials)." EPA/635/R-18/155. January. Accessed at https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=343950.

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Dr. Goodman is an expert in toxicology and epidemiology, and their application to human health risk assessments. She focuses on substances in consumer products, pharmaceuticals, and medical devices, as well as chemicals in the workplace and the environment. Dr. Goodman is board certified in toxicology, and a fellow of both the American College of Epidemiology and the Academy of Toxicological Sciences. She was also an adjunct faculty member in the Department of Epidemiology at the Harvard T. H. Chan School of Public Health, where she taught a class on meta-analysis for several years. Before joining Gradient, she was a Cancer Prevention Fellow at the National Cancer Institute. Dr. Goodman has authored numerous original peer-reviewed research articles, review articles (including systematic reviews, meta-analyses, and weight-of-evidence evaluations), and book chapters on a wide variety of chemicals and health outcomes. She has presented scientific findings and analyses at scientific and professional conferences, to community groups and regulatory and legislative bodies, and in litigation settings.

Representative Projects

Cancer Cluster Analysis: Investigated whether there was a cancer cluster in residents living near a municipal landfill. Communicated findings to city officials and residents at public meetings.

Epidemiology Analysis: Using hospital discharge and air monitoring data, conducted statistical analyses to determine the associations between air pollutants and pediatric asthma hospital admissions.

Regulatory Comment: Provided written and oral comments to several agencies and organizations (*e.g.* US EPA, National Toxicology Program) on clinical, epidemiology, toxicity, and mode-of-action studies and their bearing on regulations for pesticides, air pollutants, and other chemicals.

Post-market Safety Assessment: Evaluated whether on-label use of a pharmaceutical increased cardiovascular disease risk based on a systematic review of randomized controlled trials and observational epidemiology studies.

Product Safety Analysis: Designed and oversaw laboratory studies to determine possible exposures and subsequent toxicity of a chemical in a toy, considering several routes of exposure.

Systematic Review and Meta-analysis: Conducted a systematic review and meta-analyses of the herbicide, 2,4-dichlorophenoxyacetic acid (2,4-D), and non-Hodgkin's lymphoma (NHL), gastric cancer, and prostate cancer.

Medical Device Safety Assessment: Evaluated the potential health risks of saline-filled breast implants based on a review of the peer-reviewed literature and pre- and post-market studies of silicone- and saline-filled breast implants.

Areas of Expertise

- Epidemiology
- Toxicology
- Exposure
- Risk Assessment
- Systematic Review
- Product Safety

Education

Ph.D., Toxicology, Johns Hopkins University

Sc.M., Epidemiology, Johns Hopkins University

S.B., Environmental Engineering, Massachusetts Institute of Technology

Diplomate of the American Board of Toxicology

Fellow of the American College of Epidemiology (FACE)

Fellow of the Academy of Toxicological Sciences (ATS)

Selected Publications

Goodman, JE; Lynch, HN. 2017. "Improving the International Agency for Research on Cancer's consideration of mechanistic evidence." *Toxicol. Appl. Pharmacol.* 319:39-46.

Zu, K; Shi, L; Prueitt, RL; Liu, X; **Goodman, JE**. 2018. "Critical review of long-term ozone exposure and asthma development." *Inhal. Toxicol.* 30(3):99-113.

Zu, K; Pizzurro, DM; Lewandowski, TA; **Goodman, JE**. 2017. "Pharmacokinetic data reduce uncertainty in the acceptable daily intake for benzoic acid and its salts." *Regul. Toxicol. Pharmacol*. 89:83-94.

Goodman, JE; Peterson, MK; Hixon, ML; Shubin, SP. 2017. "Derivation of an oral maximum allowable dose level for bisphenol A." *Regul. Toxicol. Pharmacol.* 86:312-318.

Lynch, HN; Loftus; CT; Cohen, JM; Kerper, LE; Kennedy, EM; **Goodman, JE**. 2016. "Weight-of-evidence evaluation of associations between particulate matter exposure and biomarkers of lung cancer." *Regul. Toxicol. Pharmacol.* 82:53-93.