EPA'S IRIS PROGRAM: REVIEWING ITS PROGRESS AND ROADBLOCKS AHEAD

Statement of

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Chairwoman Sherrill, Chairwoman Fletcher, distinguished members of the Subcommittees, I am honored to appear before you today for this hearing entitled, "EPA's IRIS Program: Reviewing its Progress and Roadblocks Ahead." My name is Ivan Rusyn. I am Professor in the Department of Veterinary Integrative Biosciences, Chair of the Interdisciplinary Faculty of Toxicology and Director of a Superfund Research Center at Texas A&M University.

As a matter of full disclosure pertaining to the topic of today's hearings, I am currently chairing a Workshop Committee of the National Academies of Sciences, Engineering & Medicine to Support Development of EPA's IRIS Toxicological Reviews. However, I appear before you today representing my own perspectives, and not those of the National Academies, or Texas A&M University. I will offer insights from my role as a researcher in the field of toxicology and a person with understanding of the process of developing human health assessments in general, and the IRIS program in particular. I have more than a decade of service as peer reviewer of various IRIS assessments, including *Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde*, which was released in 2011. I also served as a faculty fellow to the IRIS Program for 2 years where I interacted with IRIS staff on a variety of scientific and methodological issues directly relevant to implementation of the advice from the National Academies. In addition, I reviewed a number of listings in the Report on Carcinogens by the National Toxicology Program, served on the working groups conducting human cancer hazard evaluations at the International Agency for Research on Cancer, and advise several state environmental protection agencies. My laboratory is funded by the National Institutes of Health, the Environmental Protection Agency, the National Academies, California EPA, and the European Petroleum Refiners Association. Of nearly 230 scientific publications that I have co-authored, many include colleagues in academia, government and industry. Therefore, I believe I have a good

understanding of the importance of IRIS, the challenges that this program has, and the progress that it has made in the past decade.

As requested by the Subcommittees, I am here to offer my thoughts on the progress IRIS has made addressing recommendations made by the National Academies, and the role IRIS plays in the field of chemical toxicity assessment. I also would like to use a case example of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde to highlight the challenges that IRIS is facing with timely delivery of its products and the apparent controversies with the division of responsibilities in developing chemical toxicity assessments between the offices within EPA.

The role IRIS plays in the field of chemical toxicity assessment

I begin with stating my personal opinions on the role IRIS plays in the field of chemical toxicity assessment. The history of the IRIS program and its goals have been already widely addressed and I will not re-state the well known facts. I do wish to point out the importance of the placement of this program within the Office of Research and Development, independent of the program and regional offices of the EPA. IRIS is responsible for developing toxicologic assessments of environmental chemical contaminants, these assessments contain hazard identifications and dose-response assessments and cover cancer and noncancer outcomes. It is difficult to overstate the importance of the IRIS program to the protection of public health in the United States and abroad.

It was noted by the National Research Council in 2014 that "*although [IRIS] was created to increase consistency among toxicologic assessments within [EPA], other federal agencies, various state and international agencies, and other organizations have come to rely on IRIS assessments*

for setting regulatory standards, establishing exposure guidelines, and estimating risks to exposed populations."[1] The EPA itself acknowledges the key role that IRIS-produced assessments play in many risk management decisions and Superfund site cleanup. EPA OSWER Directive 9285.7-53 states that "*IRIS remains in the first tier of the recommended hierarchy as the generally preferred source of human health toxicity values. IRIS generally contains [toxicity] values that have gone through a peer review and EPA consensus review process. IRIS normally represents the official Agency scientific position regarding the toxicity of the chemicals based on the data available at the time of the review*."[2]

The process of conducting toxicologic assessments of environmental contaminants by IRIS involves many steps, requires comprehensive and systematic review of all available evidence followed by integration and synthesis of the voluminous information. Draft assessments are subject to public comment and undergo extensive intra-governmental and external peer review. These are among the most scrutinized assessments of the potential hazardous effects of chemicals. The products are toxicity values for health effects resulting from chronic exposure to chemicals and, if the chemical was evaluated for its potential carcinogenicity in humans, a classification with respect to the chemical's potential to pose human cancer hazard. The focus of IRIS is on protecting the human population (including sensitive subgroups) under conditions of continuous inhalation or oral exposure to chemicals; therefore, IRIS values are relevant for protecting the health and wellbeing of everyone, not only those who may be exposed in the workplace, and not

[1] Review of EPA's Integrated Risk Information System (IRIS) Process. Report of the National Research Council. 2014.
[2] OSWER Directive 9285.7-53: Human Health Toxicity Values in Superfund Risk Assessments. December 05, 2003. https://www.dtsc.ca.gov/LawsRegsPolicies/Regs/upload/EPA-Tox-Criteria-Hierarchy-OSWER-Directive-9285-7-53.pdf

only by a narrow choice of the routes of exposure or conditions of use. As such, IRIS values are broadly applicable in a variety of risk management decisions.

The progress IRIS has made addressing recommendations from the National Academies

As of March 22, 2019, the IRIS program lists a total of 482 substances with assessments that derived reference dose (RfD), reference concentration (RfC), drinking water unit risk values, or inhalation unit risk values.[3] The first assessments were completed in 1987 and the most recent assessment was added in 2018. The IRIS database contains a total of 354 substances with an oral non-cancer toxicity value, 159 with an inhalation non-cancer toxicity value, and 265 with at least one of the cancer slope values. There are 22 assessments currently listed by IRIS as "*in development for which draft materials have been released to the public*."[4] The number of chemicals with an IRIS toxicity value is woefully small as compared to the estimated number of chemicals in the environment; therefore, other parts of the EPA and Federal government, as well as many States, derive similar values for chemicals of concern.

The number of chemicals with new or updated assessments by IRIS has been on a steady decline since the program released a large number of assessments in the late 1980s (Figure 1, data from[3]). It is especially obvious that the number of completed or updated assessments is particularly low since 2011, only 14 assessments have been released in 2012-2019 time period. A slow-down in the rate of assessment completion by IRIS can be due to a number of reasons, one of them is likely a 2011 National Research Council's report *Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde*. The 15-member committee that produced this report focused

[3] IRIS Advanced Search: https://cfpub.epa.gov/ncea/iris/search/index.cfm
[4] https://cfpub.epa.gov/ncea/iris_drafts/atoz.cfm?list_type=erd

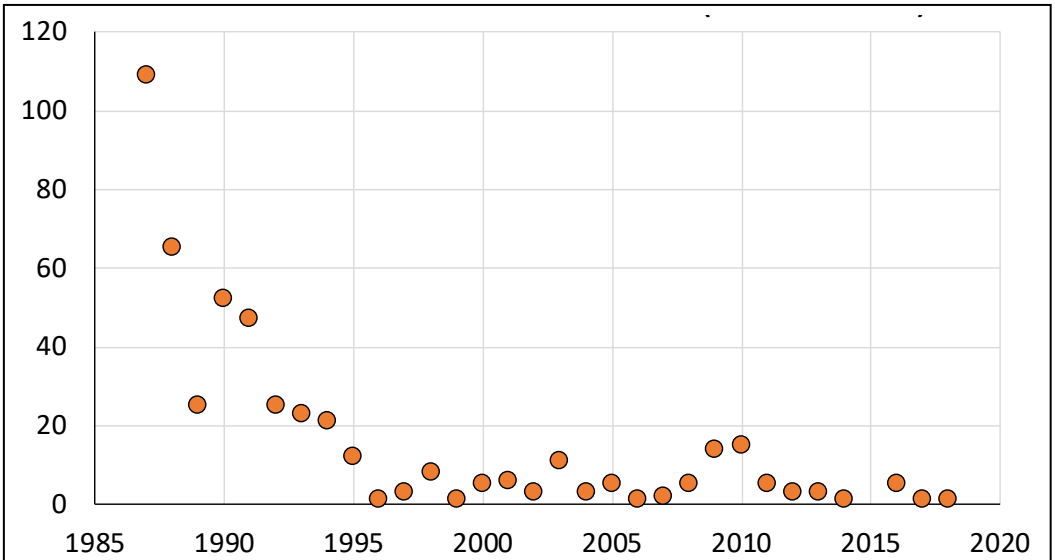

Figure 1. The number of chemicals with an IRIS assessment (y-axis) as a function of the year (x-axis) when an assessment was finalized or last revised. Data are from the online IRIS database[3] as of March 22, 2019.

on addressing specific questions related to the derivation of the RfCs for noncancer effects and of unit risk estimates for cancer from exposures to formaldehyde. In addition, the committee assessed the processes underlying the development of the IRIS assessments and made a number of suggestions on how the process can be improved and expedited. The committee identified a number of recurring methodologic problems with how IRIS assessments were developed and presented. Most of the committee's comments were on the general methodology of the assessment and the processes used by EPA to develop IRIS assessments, but not on the IRIS program itself. The committee was concerned with the persistence of the problems, particularly in light of the continued evolution of risk assessment methods and the increasing societal and legislative pressure to evaluate a greater number of chemicals in an expedient manner. The committee offered a roadmap for changes in the overall process and some more specific guidance on the steps of evidence identification, evidence review and evaluation, weight-of-evidence evaluation, selection of studies, and calculation of toxicity values. The committee recognized that

this process may take some time and that the EPA is fully capable of implementing suggested improvements, hence no delay in releasing other assessments was recommended.

Two subsequent committees of the National Academies have weighed in on the progress made by the IRIS program in implementing recommendations and improving the process. As an external peer-reviewer of the 2014 National Research Council's report *Review of EPA's Integrated Risk Information System (IRIS) Process*,[1] I fully agree with the committee's conclusion that "*the changes that EPA has proposed and implemented to various degrees constitute substantial improvements in the IRIS process.*" In 2018, the National Academies issued another report *Progress Toward Transforming the Integrated Risk Information System (IRIS) Program: A 2018 Evaluation*,[5] which concluded that "*The committee is encouraged by the steps that EPA has taken, which have accelerated during the last year under new leadership. It is clear that EPA has been responsive and has made substantial progress in implementing National Academies recommendations*." I have read this report and its appendices and fully agree with this conclusion.

Another important reason for why the productivity of IRIS is suffering, in my personal opinion, is the lack of support to this program from the EPA leadership. It is disconcerting to me that it appears that IRIS lacks sufficient financial resources and adequate staffing. As has been stated in the 2019 GAO report[6], there have been a number of recent events that may have grave long-term consequences to the ability of IRIS to continue implementation of the advice from the National Academies, to complete draft assessments, and to set priorities commensurate with the needs of

[5] Progress Toward Transforming the Integrated Risk Information System (IRIS) Program: A 2018 Evaluation. Report of the National Academies of Sciences, Engineering, and Medicine. 2018.
[6] CHEMICAL ASSESSMENTS: Status of EPA's Efforts to Produce Assessments and Implement the Toxic Substances Control Act. GAO-19-270. United States Government Accountability Office. 2019.

the other offices at the EPA and of other stakeholders. These developments are troubling and I encourage the Subcommittees to look into the GAO report's facts and conclusions to determine whether the EPA may need to support and strengthen IRIS, as suggested by the National Academies.

Overall, it is my opinion that substantial improvements in the IRIS process have been made in a relatively short period of time, and it is clear that IRIS welcomed the advice it has been receiving from the National Academies and other stakeholders. IRIS fully embraced the concept of systematic review and has become a leader in creating a process for implementation of the best practices from the systematic review in clinical medicine to environmental health. This process is neither easy, nor it is straightforward and IRIS is to be commended for their leadership. Also, a number of strategic decisions were made by the leadership of NCEA and IRIS to develop specific guidance and further standardize the process of developing the assessments. A number of software solutions have been implemented to streamline the process and facilitate teamwork. Investments in staff training and interactions with outside stakeholders were made, which further increases my personal confidence that the program is on the right track.

Formaldehyde assessment: A case study of the challenges facing IRIS

The 2011 National Research Council's report *Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde* has hastened the evolution of IRIS, a process that has been implemented with full embrace of the recommendations from several subsequent committees of the National Academies. However, it is worth reminding everyone that the 2011 report did not recommend that EPA delay the revisions and release of the formaldehyde assessment while amendments to the overall approach and process are undertaken. In fact, the

2011 committee provided specific guidance as to the steps needed to revise and finalize the draft that was presented to the Academies in 2010. Not only has the draft assessment been in development for many years before 2010, but also, very regrettably, it remains in draft form still. The formaldehyde IRIS assessment has not yet been released for public comment and moved to completion; to the contrary, some in the EPA appear to be inclined to stop this assessment by IRIS and instead conduct evaluation of formaldehyde under the Toxic Substances Control Act.[7]

Before 2016, the EPA had no mandate to review or assess the safety of chemicals already in commerce as part of TSCA. The Frank R. Lautenberg Chemical Safety for the 21st Century Act does provide that under TSCA, Office of Pollution Prevention and Toxics evaluates and regulates, as appropriate, the full life cycle, i.e., manufacture (import), distribution in commerce, use and disposal, of industrial chemicals, which includes both existing and new industrial chemicals. Therefore, formaldehyde and other existing industrial chemicals can be evaluated under TSCA; however, this evaluation should not duplicate or negate high-quality comprehensive assessments that are ready for completion under the IRIS process. In my personal opinion, the potential transfer of the formaldehyde assessment from IRIS to TSCA is a very troubling development that, at the least, will further delay the release of the assessment and establishment of public health-protective guideline toxicity values for formaldehyde exposure to the general population, including sensitive individuals. Formaldehyde is a known human carcinogen as listed in the Congress-mandated

[7] Initiation of Prioritization Under the Toxic Substances Control Act (TSCA). A Notice by the Environmental Protection Agency on 03/21/2019. 84 FR 10491. https://www.federalregister.gov/documents/2019/03/21/2019-05404/initiation-of-prioritization-under-the-toxic-substances-control-act-tsca

Report on Carcinogens[8] and as concluded by the committee of the National Research Council[9] (for full disclosure I have served as a member of the committee that produced the 2014 report[9]). Therefore, delays in completing the evaluation of this chemical are unacceptable and detrimental to the protection of public health.

Recommendations

- The IRIS program has implemented the recommendations of the National Academies, in fact, it is a leader in the evolution of risk assessment practices. Therefore, IRIS should be supported with adequate financial resources and staff.
- While important improvements are being made to the IRIS process, it is important to complete IRIS assessments that are in draft, including formaldehyde assessment, and to increase the number of evaluations that IRIS generates. These changes will need an increase in resources as compared to the current budget. IRIS is vital to public health protection in the United States and abroad.
- Congress shall strengthen oversight of the implementation of the Frank R. Lautenberg Chemical Safety for the 21st Century Act.

Thank you for the opportunity to appear before the hearing of the United States House of Representatives Committee on Science, Space and Technology Subcommittee on Investigations and Oversight and Subcommittee on Environment. I would be happy to answer any questions the members might have.

[8] NTP (National Toxicology Program). Formaldehyde. Pp. 195-205 in Report on Carcinogens, 12th Ed. U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program, Research Triangle Park, NC. 2011.
[9] Review of the Formaldehyde Assessment in the National Toxicology Program 12th Report on Carcinogens. Report of the National Research Council. 2014.