EPA's Integrated Risk Information System (IRIS) Program

Report to Congress

U.S. Environmental Protection Agency: Office of Research and Development

January 2018

Background:
In order to ensure that all Americans are protected from significant risks to their health, the U.S. Environmental Protection Agency (EPA) develops human health assessments that evaluate the potential health effects that may result from exposure to environmental contaminants. The Integrated Risk Information System (IRIS) Program helps EPA accomplish its mission by providing high quality, publicly available information on the toxicity of chemicals to which the public might be exposed. IRIS assessments are not regulations, but they provide a critical part of the scientific foundation for decision-making to protect human health across EPA under an array of environmental laws (e.g., Clean Air Act; Safe Drinking Water Act; Comprehensive Environmental Response, Compensation, and Liability Act).

For the last several years, numerous stakeholders, including industry, NGOs, state health officials, and others, have noted the importance of a strong and transparent assessment development process that produces high quality and timely products based on best available science to inform Agency decision-making. Mirroring this interest, Congress has also requested information and periodic updates on the IRIS Program's progress responding to recommendations,[1] most notably from the National Academies (NAS) National Research Council.[2, 3] In the Consolidated Appropriations Act of 2017, as well as accompanying explanatory language, Congress requested actions related to the IRIS Program's implementation: of NAS recommendations, focused on:

- Peer review for the draft IRIS assessment of formaldehyde;
- Implementation of NAS recommendations in other IRIS assessments; and,
- A review of implementation of NAS recommendations by an interagency working group.

Language from the Consolidated Appropriation Act of 2017 and accompanying explanatory statements are provided in Appendix 1 of this Report.

Purpose of This Report

Accordingly, the purpose of this report is to update Congress on the peer review status of the formaldehyde report, implementation of NAS recommendations in assessments other than formaldehyde, and the efforts of an interagency working group to evaluate implementation of the NAS recommendations.

Peer Review for the IRIS Formaldehyde Assessment

Within the funds provided, EPA has contracted the NAS to conduct the peer review of the revised draft IRIS assessment of formaldehyde. The draft report will go through the formal

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[1] Copies of previous EPA progress reports and reports to congress are available at: https://www.epa.gov/iris/iris-progress-reports.
[2] *Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde*. Available from - http://www.nap.edu/catalog/13142/review-of-the-environmental-protection-agencys-draft-iris-assessment-of-formaldehyde
[3] *Review of EPA's Integrated Risk Information System (IRIS) Process.* Available from - http://www.nap.edu/catalog/18764/review-of-epas-integrated-risk-information-system-iris-process

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review process which will involve public comment before delivery to the NAS for peer review. In this draft report, EPA has implemented the systematic review recommendations of the 2011 and 2014 NAS reports, including standardized and transparent evaluation of the strengths and weaknesses of critical studies, a strengthened and more integrative weight-of-evidence evaluation, and clearer rationale for selecting the studies that are advanced for consideration in calculating toxicity values. The draft also addresses the recommendations and considerations specific to evaluating the hazards of formaldehyde. IRIS plans to deliver an External Review Draft of its Formaldehyde Assessment for public comment and peer review in FY 2018.

Other IRIS Assessments

Systematic review is a structured and documented process for transparent literature review. It is "a scientific investigation that focuses on a specific question and uses explicit, pre-specified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies. The goal of systematic review methods is to ensure that the review is complete, unbiased, reproducible, and transparent.[4,5]" Systematic review science is rapidly evolving in its application to environment and public health fields. The primary recommendations of the 2011 and 2014 NAS reports related to IRIS's implementation of systematic review, and specifically as it relates to clear and objective presentation of the strengths and weaknesses of critical studies, evidence evaluation and synthesis, and selection of key studies to calculate toxicity values.

Over the last several years, the IRIS Program has been exploring how to practically implement systematic review into chemical assessment.[6] For example, all draft and final EPA assessments prepared by IRIS in fiscal year (FY) 2017 described considerations for judging the strengths and weaknesses of all key studies and a description of how the evidence was integrated. During FY 2017, and with the arrival of the new IRIS Director who is a global leader in systematic review, IRIS began to fully operationalize systematic review pragmatically across all its assessment products. The most recent processes used to assess the quality of studies and conduct the evidence integration were shared with the public during a September 27-28, 2017 meeting with the Science Advisory Board Chemical Assessment Advisory Committee (SAB-CAAC). As IRIS has operationalized systematic review, information pertaining to assessments have been made available for public review and comment earlier in the assessment development process, providing ample time for consideration of the scientific complexities before the assessment is drafted.

The IRIS Interagency Working Group and Review of NAS Recommendation Implementation

IRIS convened its Interagency Working Group (IWG) in August 2017 with the added responsibility of addressing these report recommendations. This specific IWG effort is co-

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[4] Institute of Medicine. Finding What works in Health Care: Standards for Systematic Reviews. p.13-34. The National Academies Press. Washington, D.C. 2011.

[5] Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act. EPA-HQ-OPPT-2016-0654. https://www.epa.gov/sites/production/files/2017-06/documents/prepubcopy_tsca_riskeval_final_rule_2017-06-22.pdf

[6] Previous workshops on systematic review that were open to stakeholders and the public were held in August 2013, October 2014, and December 2015.

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chaired by EPA and the Office of Information and Regulatory Affairs (OIRA) in the Office of Management and Budget (OMB). The IWG includes relevant executive branch stakeholders, from Small Business Administration, Department of Health and Human Services, Department of Energy, Department of Defense, National Aeronautics and Space Administration, Department of Agriculture, Department of Veterans Affairs, White House Offices of Management and Budget and Council on Environmental Quality, Department of Labor, and Consumer Products Safety Commission.

In FY 2017, the IWG met three times from August to September. In these early meetings, the IWG received a briefing on the status of the IRIS Program from key staff and the new National Center for Environmental Assessment (NCEA) and IRIS Program Directors, who began their tenures in January 2017:

- **NCEA Center Director:** With significant experience in the chemical industry, and formerly the Director of ORD's Chemical Safety for Sustainability National Research Program, the new NCEA Director brings knowledge of TSCA, innovative applications of computational toxicology, and exposure science.
- **IRIS Program Director:** As a recognized leader in systematic review, automation, and chemical evaluations, the new IRIS Program Director brings experience in early partner and stakeholder engagement and input, and demonstrated actions to increase capacity and transparency in assessments.

IRIS reported to the IWG on other program improvements to:

- **Increase the transparency of assessments by fully implementing the principles of systematic review**
  - The IRIS Program has adapted or developed standardized approaches that foster consistency across the IRIS Program; enabling active and new assessments to meet <u>all</u> systematic review-related recommendations from the 2011 and 2014 NAS reports.
  - Developing standard operating procedures (IRIS Handbook) and chemical assessment-specific protocols that provide consistency across assessments.
- **Modernize the IRIS Program.** The IRIS Program is developing and using automation and machine-learning tools to expedite systematic review and incorporate emerging data types.
- **Modularize product lines.** IRIS implemented a portfolio of chemical evaluation products that optimize the application of the best available science and technology. These products will allow IRIS to remain flexible and responsive to customers within EPA as well as the diverse stakeholders beyond EPA, including states, tribal nations, and other federal agencies.
- **Enhance accessibility**
  - IRIS is providing outreach and training within and outside EPA to build familiarity and acceptance of systematic review practices.
  - Promote data sharing through publicly available software platforms for assessments developed by EPA, other federal and state agencies, industry, academia and other third-parties.

The IRIS IWG agreed to continue to meet on a quarterly basis beyond FY 2017 to remain aware of the implementation status of NAS recommendations, be updated about future interactions with

the NAS (see below), as well as be informed on longer-term, research-driven recommendations (e.g., advancing analytical and quantitative techniques such as Bayesian methods). These ongoing activities will enhance Federal agency coordination and application of evolving risk assessment methodologies.

Future NAS Review of the IRIS Program

Along with the efforts described above, to further address Congress's concerns EPA has requested that the National Academies convene a public meeting and independently review the progress of the IRIS Program in implementing the 2014 NAS recommendations. The NAS will convene a committee in FY 2018, and issue a consensus report within six months. This report will also inform the ongoing activities of the IWG.

Conclusion

Previous reports to Congress have described the progress the IRIS Program has made. Consistent with these efforts, the 2017 GAO High Risk report noted significant improvement in their high risk criteria ratings specific to the IRIS Program. EPA is committed to ensuring that the IRIS Program provides high-quality assessments that adhere to the highest standards of scientific integrity, and that are both transparent and timely. Through our past and continuing actions to improve the IRIS Program, we are ensuring that the foundation for Agency decisions to protect human health is based on the best available science.

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Appendix 1

IRIS-Relevant Congressional Language from the Consolidated Appropriations Act of 2017

From FY 2017 Budget Explanatory language[7]

> *Integrated Risk Information System (IRIS).* —The Committees are aware of efforts to implement the 2011 National Academy of Science' s (NAS) Chapter 7 and 2014 NAS report recommendations for the IRIS Program, including six specific recommendations. These recommendations include objective evaluation of the strengths and weaknesses of critical studies, the need for weight of evidence evaluation and integration, and clearer rationale for selecting studies to calculate toxicity values. Additionally, the NAS identified specific recommendations and considerations when evaluating the hazards of formaldehyde. The Committees believe that EPA should contract with the NAS to conduct the peer review of the revised draft IRIS assessment of formaldehyde, should it be released in fiscal year 2017, to verify the recommendations from the previous NAS report of 2011 have been fully resolved scientifically.

From House Report 114-632[8]

> Within the funds provided, $1,000,000 shall be used to contract with the National Academy of Sciences (NAS) to conduct the peer review of the revised draft IRIS assessment of formaldehyde. The NAS shall ensure that all recommendations and concerns raised in the April 2011 report of the NAS are fully resolved scientifically in the revised draft assessment.
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> Additional Guidance. —The Committee has included the following additional guidance with respect to funding provided under this account:
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> Integrated Risk Information System (IRIS) and other assessments. —At least six critical recommendations from the National Academy of Sciences (NAS) have yet to be implemented including objective evaluation of the strengths and weaknesses of critical studies, the need for weight of evidence evaluation and integration, and clearer rationale for selecting studies to calculate toxicity values. Additionally, the NAS identified specific concerns that need to be addressed when evaluating the hazards of formaldehyde. The Committee believes it is essential for the NAS to peer review the revised draft assessment of formaldehyde to verify whether EPA has addressed all previous recommendations.
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> In addition, for all draft or final EPA risk assessments issued in fiscal year 2017, the Committee directs the Agency to provide clear criteria for judging the quality of all key studies and to provide a description of how all evidence will be integrated, based on its strengths and weaknesses, in advance of releasing any future draft assessments. When evaluating the potential carcinogenic effects of substances, the Agency shall also present non-linear modeling approaches. Consistent with EPA's Risk Characterization Handbook (U.S. EPA, 2002), draft and final hazard and exposure assessments, produced by EPA offices, should also include the distribution of estimated hazards, exposures, or risks, including central tendency values.

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[7] https://www.congress.gov/crec/2017/05/03/CREC-2017-05-03-bk2.pdf
[8] https://www.congress.gov/congressional-report/114th-congress/house-report/632/1

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From Senate Report 114-281[9]:

Within the funds provided, $1,000,000 shall be used to contract with the National Academy of Sciences [NAS] to conduct the peer review of the revised draft IRIS assessment of formaldehyde. The review shall ensure that all recommendations and concerns raised in the April 2011 report of the NAS are fully addressed in the revised draft assessment.

Integrated Risk Information System. —The Committee is aware of efforts by the Agency to implement the 2011 National Academy of Science's [NAS] Chapter 7 and 2014 NAS report recommendations for the Integrated Risk Information System [IRIS] but remains concerned that the recommendations have not been fully implemented. In published appendices that accompany final IRIS assessments, EPA has detailed some of the Agency's deficiencies in meeting the NAS high-priority reforms. The Committee directs the Agency to convene an interagency working group to be Co-Chaired with the Office of Information and Regulatory Affairs and to include relevant executive branch stakeholders to review compliance with the NAS recommendations in IRIS assessments issued since the 2014 NAS report. The working group shall focus specifically on transition from the use of single point estimates of hazard and exposure to presenting more complete information on the distribution of estimated hazards, exposures, and/or risks, including central tendency values; on processes for evaluating study quality, relevance, and risk of bias; the use of a transparent and reproducible weight-of-evidence process for applying scientific findings; the selection of an adverse outcome; and the use of default linear low-dose extrapolation and other default modeling approaches to hazard determinations. The Committee directs the Agency to issue a report to the Committees of Appropriations of the House and Senate on the findings of the working group and the implementation plans of its findings within 180 days of enactment of this act. The working group report shall also include a timetable for EPA's full implementation of the NAS recommendations for all IRIS assessments issued since the 2014 NAS report.

[9] https://www.congress.gov/congressional-report/114th-congress/senate-report/281/1