U.S. House of Representatives
Committee on Science, Space, and Technology
Subcommittee on Investigations & Oversight

HEARING CHARTER

"EPA's IRIS Program: Evaluating the Science and Process Behind Chemical Risk Assessment"

Thursday, July 14, 2011
10:00 a.m. – 12:00 p.m.
2318 Rayburn House Office Building

Purpose

On July 14, 2011, the Subcommittee on Investigations and Oversight will hold a hearing on the U.S. Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS). There will be two panels at the hearing; the first panel will comprise of witnesses from EPA, the U.S. Government Accountability Office (GAO), and the National Academies' National Research Council. The second panel will include individuals and experts who will talk about their perspectives on IRIS.

In March of 2008, GAO reported that "the IRIS database was at serious risk of becoming obsolete because EPA had not been able to routinely complete timely, credible assessments. After subsequent reports, in January 2009 [GAO] added EPA's processes for assessing and controlling toxic chemicals to [its] list of areas at high risk for waste, fraud, abuse, and mismanagement or in need of broad-based transformation."[1]

As a result, the Subcommittee held several hearings on this subject. On May 21, 2008, the Subcommittee took testimony from Dr. George Gray, the then-Assistant Administrator for Research and Development at EPA, and Ms. Susan Dudley, the then-Administrator of the Office of Information and Regulatory Affairs (OIRA). Additionally, Mr. John Stephenson of GAO testified on findings regarding the lack of productivity in the IRIS process.

On June 12, 2008, the Subcommittee received testimony from Mr. Jerry Ensminger (U.S.M.C., retired), Mr. Lenny Seigel (Executive Director, Center for Public Environmental Oversight), and Dr. Linda Greer (Director of the Health Program at the Natural Resources Defense Council).

In 2009, the Subcommittee heard from Mr. John Stephenson again, and Dr. Kevin Teichman, the Deputy Assistant Administrator for Science at EPA's Office of Research and Development. They testified about the current IRIS process announced by EPA Administrator Lisa Jackson on May 21, 2009.

[1] David Trimble, Director, Natural Resources and Environment, Testimony before the Subcommittee on Investigations and Oversight, Committee on Science, Space, and Technology, July 14, 2011

These prior IRIS hearings focused on the IRIS interagency review process, and delved into the role of the White House and other agencies, to determine the extent of their involvement in IRIS' chemical risk assessments. Today's hearing, prompted in part by the National Academies' National Research Council report on EPA's formaldehyde assessment, focuses on the process EPA uses to initially develop draft IRIS assessments, which is separate from the overall process that includes the multiple layers of review. The National Academy of Sciences' (NAS) report dedicated an entire chapter that reiterated several previous criticisms of EPA's IRIS process. In light of those criticisms, and recognizing that this is not the first time NAS has articulated them, the committee's goal is to better understand the process behind the development of IRIS' chemical risk assessments, whether EPA plans on adopting the NAS' recommendations, and whether or not EPA assessments are based on the best available evidence and evaluated in accordance with established protocols.

Background

IRIS was established in the 1980s as an internal EPA database to provide a single source of information on the risks associated with exposure to chemicals. The IRIS database provides a hazard identification and dose-response analysis, scientific information that when combined with estimates of exposure allow regulatory agencies to produce a risk assessment. Historically, entries to the database were the result of extensive in-house development by the science staff at EPA, peer review processes with experts from outside the agency, and opportunities for public input and comment.

By the early 1990s, the chemical database contained information on roughly 500 chemicals. However, as IRIS grew and gained more influence, EPA decided to restructure the IRIS process, which unfortunately led to the demise of the heretofore successful collaborative platform. This restructuring ultimately led to several reorganizations of the IRIS process (*see Appendix B*), with the most recent one announced by EPA Administrator Lisa Jackson on May 21, 2009.

In 2009, GAO testified before this Subcommittee that EPA "has not been able to complete timely, credible chemical assessments or decrease its backlog of 70 [as of 2008] ongoing assessments."[2] Further, GAO reported, "because EPA staff time was dedicated to completing assessments in the backlog, EPA's ability to both keep the more than 540 existing assessments up to date and initiate new assessments was limited. We found that 48 of the 70 assessments being conducted as of December 2007 had been in process for more than 5 years—and 12 of those, for more than 9 years. These time frames have lengthened. Currently, of those 70 assessments, 58 have now been ongoing for more than 5 years—and 31 of those for more than 9 years."[3]

The IRIS database currently includes 554 chemicals. Since GAO last reported, EPA completed six assessments in 2009 and ten assessments in 2010.[4] These numbers are far below the twenty

[2] John B. Stephenson, Director, Natural Resources and Environment, Testimony before the Subcommittee on Investigations and Oversight, Committee on Science and Technology, June 11, 2009
[3] Ibid.
[4] "Update on Integrated Risk Information System (IRIS) Program Activities," EPA, Office of Research and Development, National Center for Environmental Assessment (NCEA) (hereinafter NCEA IRIS document)

assessments EPA planned to finalize in 2010. Moreover, 70 chemicals continue to remain in various stages of review.

Further compounding the problem, EPA line offices are no longer required to concur with IRIS assessments and internal EPA comments are still not transparent. The quality of assessments being produced also continues to be an issue. Since 2005, five assessments have been referred to the National Academies' for evaluation. All of the NAS reviews have severely criticized EPA's assessments, and offered numerous recommendations, which EPA has yet to implement.

Issues

NAS: "Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde"

On April 8 of this year, NAS published its long-awaited study on EPA's formaldehyde assessment. While NAS "strongly questioned EPA claims that exposure to formaldehyde can result in increased risk of a leukemia and other cancers that had not previously been associated with formaldehyde, asthma, and reproductive toxicity,"[5] that is not the most compelling part of the document for the purposes of this hearing. Of interest is that the NAS panel "strongly faulted EPA's methodology in crafting its draft assessment, warning of a pattern of problems in how the agency crafts assessments for its Integrated Risk Information System (IRIS) database that could continue to hamper future risk studies. 'The committee is concerned about the persistence of problems encountered with IRIS assessments over the years, especially given the multiple groups that have highlighted them...If the methodologic issues are not addressed, future assessments may still have the same general and avoidable problems that are highlighted here.'"[6]

In the summary of the report, the panel commented on the similarities in some of the problems with the IRIS assessment on formaldehyde, and those identified in other reports published by previous NAS panels:

> "Overall, the committee noted some recurring methodologic problems in the draft IRIS assessment of formaldehyde. Many of the problems are similar to those which have been reported over the last decade by other NRC committees tasked with reviewing EPA's IRIS assessments for other chemicals. Problems with clarity and transparency of the methods appear to be a repeating theme over the years, even though the documents appear to have grown considerably in length. In the roughly 1,000-page draft reviewed by the present committee, little beyond a brief introductory chapter could be found on the methods for conducting the assessment. Numerous EPA guidelines are cited, but their role in the preparation of the assessment is not clear. In general, the committee found that the draft was not prepared in a consistent fashion; it lacks clear links to an underlying conceptual framework; and it does not contain sufficient documentation on methods and criteria for identifying evidence from epidemiologic and experimental studies, for

[5] Maria Hegstad, "NAS Sets Back EPA Proposal For Strict Formaldehyde Risk Assessment," Environmental NewsStand, April 8, 2011
[6] Ibid.

> critically evaluating individual studies, for assessing the weight of evidence, and for selecting studies for derivation of the RfCs and unit risk estimates."[7]

Please see Appendix A for detailed recommendations from the NAS report.

NAS: "Science and Decisions: Advancing Risk Assessment"[8]

Dr. Thomas Burke, associate dean of The Johns Hopkins Bloomberg School of Public Health, recently chaired an NAS panel on "ways to improve EPA risk assessments."[9] At a joint meeting of EPA's Science Advisory Board and EPA's Board of Scientific Counselors, Dr. Burke said, "The sleeping giant is that EPA science is on the rocks . . . if you fail, you become irrelevant, and that is kind of a crisis."[10] Referring to EPA's risk assessment process as the agency's "Achilles heel,"[11] Dr. Burke's NAS panel suggested steps on how EPA could improve that process in a 2009 report titled, "Science and Decisions: Advancing Risk Assessment." This report carries added weight in light of the NAS report on formaldehyde issued earlier this year with its chapter critical of EPA's IRIS process.

NTP's RoC

The Department of Health and Human Services' (HHS) National Toxicology Program (NTP) publishes a report every Congress called the Report on Carcinogens (RoC).[12] On June 10 of this year, the Twelfth RoC was released, and it elevated its classification of formaldehyde from 'reasonably anticipated to be a human carcinogen' to 'known to be a human carcinogen.' The report was published despite the NAS review. This is important because according to an analytic paper, NTP has:

> "been reviewing the scientific data for formaldehyde in preparation for a listing decision in the 12th Report on Carcinogens (RoC). EPA and the NTP have had available, reviewed and relied upon the same studies, reports and underlying data in conducting their respective hazard evaluations of the possible relationship between formaldehyde exposure and leukemia and other lymphohematopoietic malignancies. **Therefore, the NRC committee's review of and conclusions concerning the draft EPA IRIS report are, with respect to lymphohematopoietic malignancies (including myeloid**

[7] "Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde," National Research Council of the National Academies, April 8, 2011 (hereinafter NAS Formaldehyde Report)
[8] "Science and Decisions: Advancing Risk Assessment," National Research Council of the National Academies, 2009
[9] "Key Advisor Warns EPA to Improve Agency Science or Face a 'Crisis,'" InsideEPA.com, July 8, 2011
[10] Ibid.
[11] Ibid.
[12] Maria Hegstad, "NAS Critique of EPA Formaldehyde Study Hampers HHS 'Cancer' Report," Environmental NewsStand, April 26, 2011. "Congress directed the program to prepare the report every other year, but due to concerns over the review process for the document, the last RoC was published in 2005. The RoC provides information on chemicals that NTP deems carcinogenic or reasonably anticipates to be human carcinogens, along with people's potential for exposure to them."

> **leukemia), directly applicable to the NTP's own review and conclusions - precisely because the draft EPA and NTP reports involve the same studies and data sets.**"[13]

Further:

> "The NRC committee's opinion was that EPA's review of the scientific literature as presented in the draft IRIS assessment does not provide a sufficient scientific basis for concluding that there is a causal link between formaldehyde exposure and leukemia. The NRC committee's conclusions concerning EPA's assessment of leukemia apply as well to application of the 'listing criteria' for formaldehyde in the NTP's 12th RoC**. In particular, there is no reasonable basis for the NTP to conclude that formaldehyde should be listed in the 12th RoC as being either 'known' or 'reasonably anticipated' to cause myeloid leukemia or any other lymphohematopoietic malignancy."**[14]

The RoC's more serious listing of formaldehyde could possibly influence EPA's own assessment relating to formaldehyde and leukemia, despite NAS' comments. Conversely, if EPA reassesses its formaldehyde review and comes to a different conclusion, then that raises questions about conflicting information from two different government entities, which may cause confusion downstream as risk managers and regulators try to understand which determination is more reliable.

EPA's SAB

Under the current process, EPA's Science Advisory Board (SAB) is responsible for peer reviewing EPA's IRIS assessments. However, "there have been questions in the past, including some raised by [EPA's] Inspector General about the independence of the SAB panels."[15] [16] The charge questions that lead SAB peer reviews are "written by the EPA office requesting the review and which industry says can narrow the focus of the reviews. Sources also say the panels do not include a broad-enough roster of experts. For example, the SAB panel that recently reviewed EPA's IRIS assessment for inorganic arsenic...did not include a statistician or a cancer modeling expert and only one epidemiologist."[17]

IRIS Assessments are not Insulated from Risk Management

In the NAS' 1983 report, "Risk Assessment in the Federal Government: Managing the Process," the National Research Council panel identified four components of a complete risk assessment:

- hazard identification;
- dose-response evaluation;

[13] "National Research Council Report on Scientific Evidence Pertaining to the Relationship Between Formaldehyde Exposure and Leukemia: Implications for the National Toxicology Program's Listing of Formaldehyde in the 12th Report on Carcinogens," Environ International Corporation, April 22, 2011 (emphasis in original text)
[14] Ibid. (emphasis in original text)
[15] Aaron Lovell, "Rebuffed by EPA, Industry Asks OMB, GOP to Fix Chemical Study Process," Environmental NewsStand.com, June 22, 2011 (hereinafter Lovell Article)
[16] U.S. EPA Office of Inspector General, "EPA can Improve its Process for Establishing Peer Review Panels," Evaluation Report No. 09-P-0147, April 29, 2009
[17] Lovell Article, *supra*, note 11

- exposure assessment; and
- risk characterization.[18]

IRIS reflects science that addresses the first two conditions. In discussing the difference between risk assessment and risk management, the Academy panel wrote:

> "Risk assessment is the use of the factual base to define the health effects of exposure of individuals or populations to hazardous materials and situations. Risk management is the process of weighing policy alternatives and selecting the most appropriate regulatory action, integrating the results of risk assessment with engineering data and with social, economic and political concerns to reach a decision."[19]

This distinction is commonly cited when IRIS assessments are criticized. When assessments make determinations that safe levels are below background levels, the IRIS program can reasonably claim that such factors can be weighed later in the risk management process. In reality, IRIS assessments are usually adopted with no further consideration. "[S]ome customers use IRIS because it is a useful source of information; while for other customers IRIS is mandatory, and those customers include state agencies. Customers who use IRIS for general information often rely upon other databases to complement an IRIS assessment. Other databases exist, which can provide some help, but for domestic regulatory purposes there is no satisfactory alternative to IRIS. And using an IRIS file as the scientific basis for a regulatory decision is expected and seldom challenged."[20]

Witnesses

Panel 1

- The Honorable Paul Anastas, Assistant Administrator, Office of Research and Development, U.S. Environmental Protection Agency. Dr. Anastas will talk about EPA's efforts to implement the most recent revised IRIS process, provide a status of assessments, and discuss EPA's efforts to implement NAS' and GAO's recommendations.

- Mr. David Trimble, Director, Natural Resources and Environment, U.S. Government Accountability Office. Mr. Trimble will provide an overview of IRIS, highlight previous GAO work on IRIS, and evaluate EPA's efforts to implement GAO's recommendations.

- Dr. Jonathan M. Samet, MD, MS, Professor and Flora L. Thornton Chair, Department of Preventive Medicine, Keck School of Medicine, University of Southern California; and Chair, Committee to Review EPA's Draft IRIS Assessment of Formaldehyde, National Research Council, The National Academies. Dr. Samet will highlight the NAS' recent

[18] National Research Council, National Academy of Sciences, "Risk Assessment in the Federal Government: Managing the Process,"1983
[19] Ibid.
[20] Jim Solyst, "Eyeballing IRIS," The Environmental Forum, March/April 2009, Vol 26, No. 2

work on IRIS, and detail NAS' recommendations contained in chapter seven of their recently release report on formaldehyde.

Panel 2

- The Honorable Calvin Dooley, President and Chief Executive Officer, American Chemistry Council. Mr. Dooley will talk about IRIS and industry's perspective on the IRIS process.

- Ms. Rena Steinzor, Professor, University of Maryland School of Law, and President, Center for Progressive Reform. Ms. Steinzor will talk about IRIS, and offer suggestions on how to improve it and remove it from GAO's high risk series.

- Dr. Gail Charnley, Principal, HealthRisk Strategies. Dr. Charnley will talk about IRIS, offer suggestions on how to improve it and remove it from GAO's high risk series, and discuss the NAS' recommendations.

- The Honorable J. Christian Bollwage, Mayor, City of Elizabeth, New Jersey. Mayor Bollwage will talk about how IRIS assessments impact local communities, particularly Elizabeth, New Jersey.

Appendix A[21]

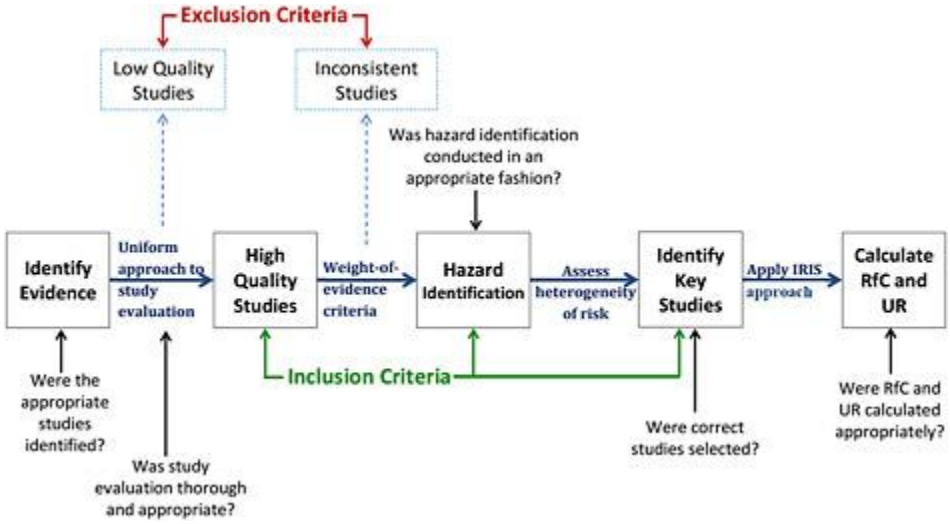


FIGURE 7-2 Elements of the key steps in the development of a draft IRIS assessment. Abbreviations: IRIS, Integrated Risk Information System; RfC, reference concentration; and UR, unit risk.

Reframing the Development of the IRIS Assessment

The committee was given the broad charge of reviewing the formaldehyde draft IRIS assessment and also asked to consider some specific questions. In addressing those questions, the committee found, as documented in Chapter 2, that some problems with the draft arose because of the processes and methods used to develop the assessment. Other committees have noted some of the same problems. Accordingly, the committee suggests here steps that EPA could take to improve IRIS assessment through the implementation of methods that would better reflect current practices. The committee offers a roadmap for changes in the development process if EPA concludes that such changes are needed. The term *roadmap* is used because the topics that need to be addressed are set out, but detailed guidance is not provided because that is seen as beyond the committee's charge. The committee's discussion of a reframing of the IRIS development process is based on its generic representation provided in Figure 7-2. The committee recognizes that the changes suggested would involve a multiyear process and extensive effort by the staff of the National Center for Environmental Assessment and input and review by the EPA Science Advisory Board and others. The recent revision of the NAAQS review process provides an example of an overhauling of an EPA evidence-review and risk-assessment process that took about 2 years.

In the judgment of the present and past committees, consideration needs to be given to how each step of the process could be improved and gains made in transparency and efficiency. Models for conducting IRIS reviews more effectively and efficiently are available. For each of the various components (Figure 7-2), methods have been developed, and there are exemplary approaches in

[21] NAS Formaldehyde Report, *supra*, note 7. The following information is available in Chapter 7 of the report.

assessments carried out elsewhere in EPA and by other organizations. In addition, there are relevant examples of evidence-based algorithms that EPA could draw on. Guidelines and protocols for the conduct of evidence-based reviews are available, as are guidelines for inference as to the strength of evidence of association and causation. Thus, EPA may be able to make changes in the assessment process relatively quickly by drawing on appropriate experts and selecting and adapting existing approaches.

One major, overarching issue is the use of weight of evidence in hazard identification. The committee recognizes that the terminology is embedded in various EPA guidelines (see Appendix B) and has proved useful. The determination of weight of evidence relies heavily on expert judgment. As called for by others, EPA might direct effort at better understanding how weight-of-evidence determinations are made with a goal of improving the process (White et al. 2009).

The committee highlights below what it considers critical for the development of a scientifically sound IRIS assessment. Although many elements are basic and have been addressed in the numerous EPA guidelines, implementation does not appear to be systematic or uniform in the development of the IRIS assessments.

General Guidance for the Overall Process

- Elaborate an overall, documented, and quality-controlled process for IRIS assessments.
- Ensure standardization of review and evaluation approaches among contributors and teams of contributors; for example, include standard approaches for reviews of various types of studies to ensure uniformity.
- Assess disciplinary structure of teams needed to conduct the assessments.

Evidence Identification: Literature Collection and Collation Phase

- Select outcomes on the basis of available evidence and understanding of mode of action.
- Establish standard protocols for evidence identification.
- Develop a template for description of the search approach.
- Use a database, such as the Health and Environmental Research Online (HERO) database, to capture study information and relevant quantitative data.

Evidence Evaluation: Hazard Identification and Dose-Response Modeling

- Standardize the presentation of reviewed studies in tabular or graphic form to capture the key dimensions of study characteristics, weight of evidence, and utility as a basis for deriving reference values and unit risks.
- Develop templates for evidence tables, forest plots, or other displays.
- Establish protocols for review of major types of studies, such as epidemiologic and bioassay.

Weight-of-Evidence Evaluation: Synthesis of Evidence for Hazard Identification

- Review use of existing weight-of-evidence guidelines.
- Standardize approach to using weight-of-evidence guidelines.
- Conduct agency workshops on approaches to implementing weight-of-evidence guidelines.

- Develop uniform language to describe strength of evidence on noncancer effects.
- Expand and harmonize the approach for characterizing uncertainty and variability.
- To the extent possible, unify consideration of outcomes around common modes of action rather than considering multiple outcomes separately.

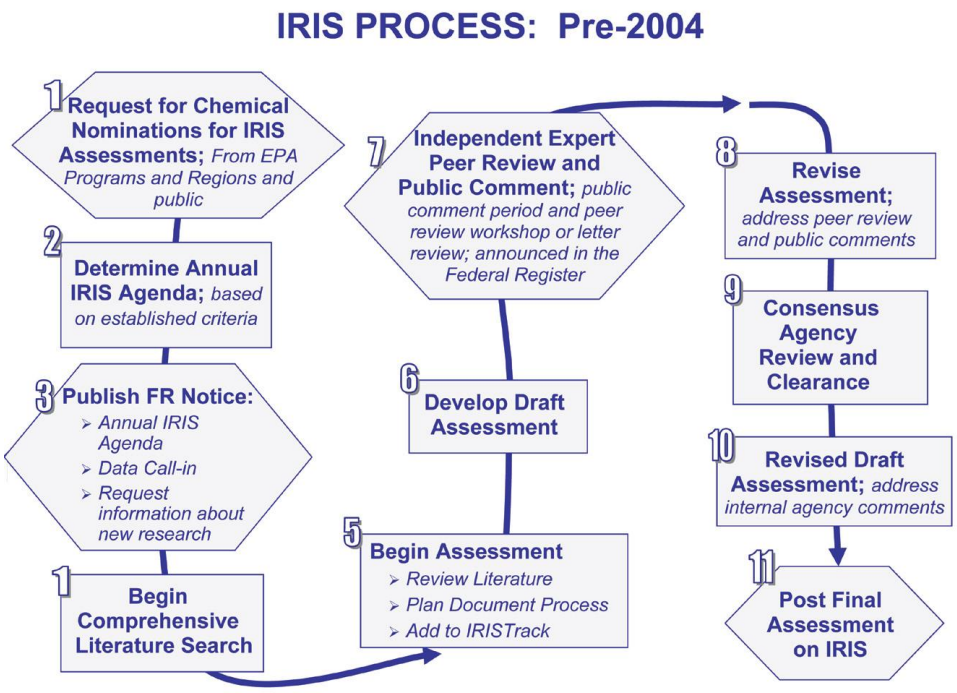
Selection of Studies for Derivation of Reference Values and Unit Risks

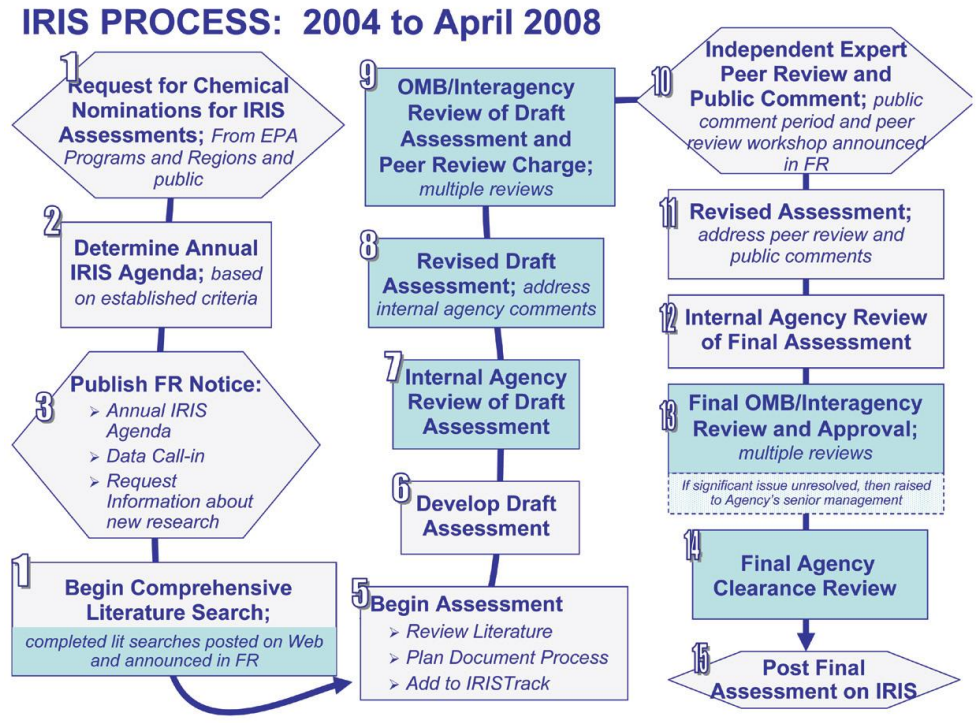
- Establish clear guidelines for study selection.
  - Balance strengths and weaknesses.
  - Weigh human vs experimental evidence.
  - Determine whether combining estimates among studies is warranted.

Calculation of Reference Values and Unit Risks

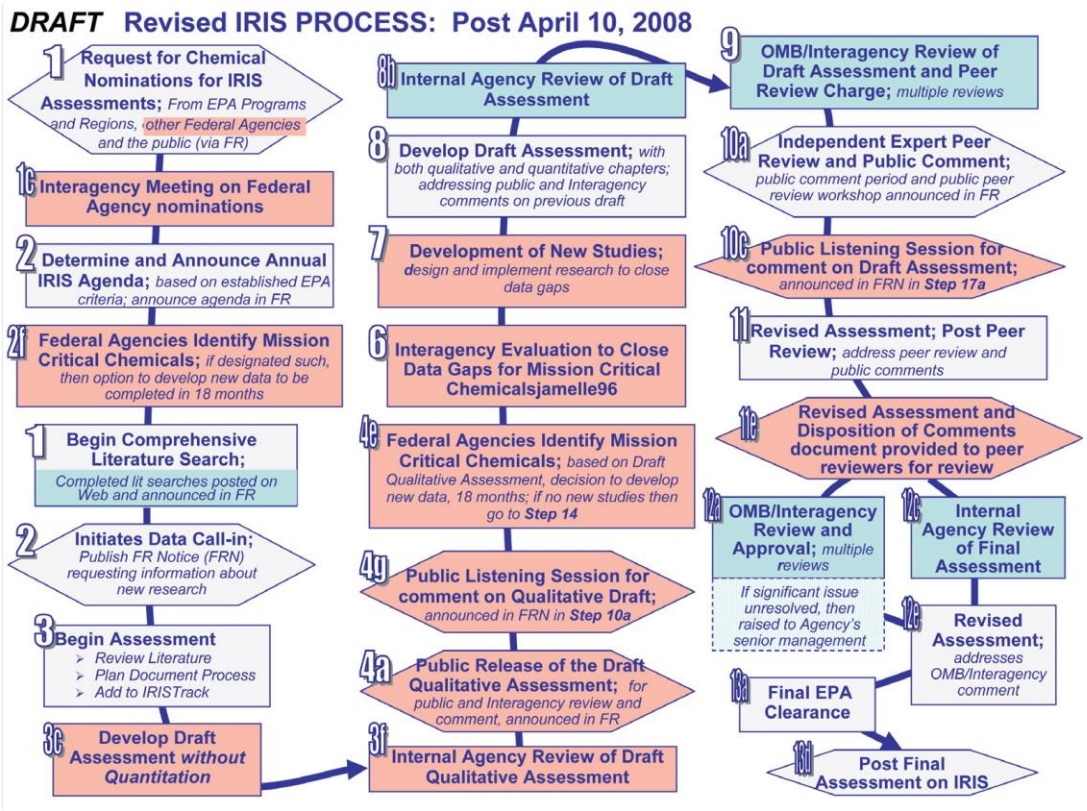
- Describe and justify assumptions and models used. This step includes review of dosimetry models and the implications of the models for uncertainty factors; determination of appropriate points of departure (such as benchmark dose, no-observed-adverse-effect level, and lowest observed-adverse-effect level), and assessment of the analyses that underlie the points of departure.
- Provide explanation of the risk-estimation modeling processes (for example, a statistical or biologic model fit to the data) that are used to develop a unit risk estimate.
- Assess the sensitivity of derived estimates to model assumptions and end points selected. This step should include appropriate tabular and graphic displays to illustrate the range of the estimates and the effect of uncertainty factors on the estimates.
- Provide adequate documentation for conclusions and estimation of reference values and unit risks. As noted by the committee throughout the present report, sufficient support for conclusions in the formaldehyde draft IRIS assessment is often lacking. Given that the development of specific IRIS assessments and their conclusions are of interest to many stakeholders, it is important that they provide sufficient references and supporting documentation for their conclusions. Detailed appendixes, which might be made available only electronically, should be provided when appropriate.

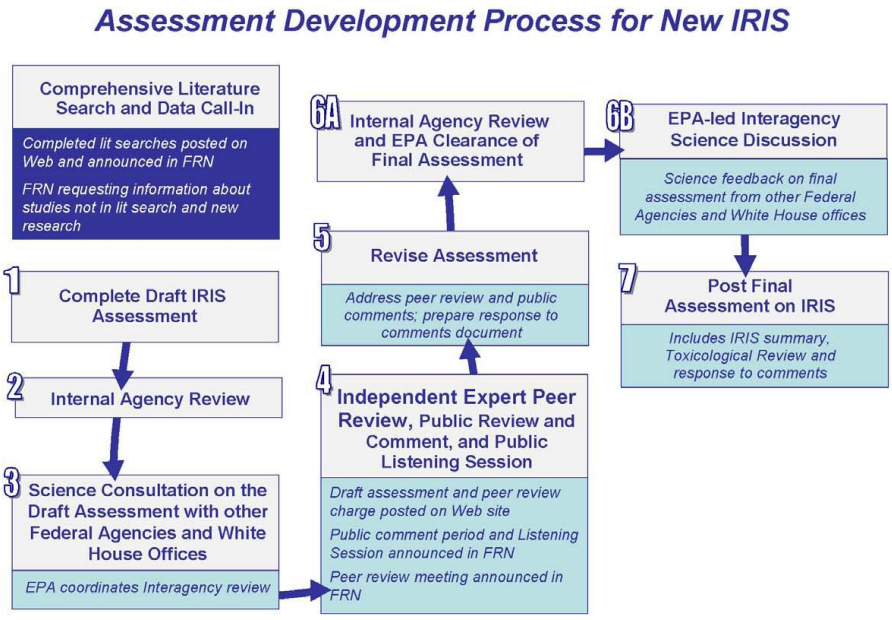
Appendix B[22]





[22] These figures are from EPA.


DRAFT Revised IRIS PROCESS: Post April 10, 2008
1 Request for Chemical Nominations for IRIS Assessments; From EPA Programs and Regions, other Federal Agencies and the public (via FR)
1c Interagency Meeting on Federal Agency nominations
2 Determine and Announce Annual IRIS Agenda; based on established EPA criteria; announce agenda in FR
2f Federal Agencies Identify Mission Critical Chemicals; if designated such, then option to develop new data to be completed in 18 months
1 Begin Comprehensive Literature Search; Completed lit searches posted on Web and announced in FR
2 Initiates Data Call-in; Publish FR Notice (FRN) requesting information about new research
3 Begin Assessment
Review Literature
Plan Document Process
Add to IRISTrack
3c Develop Draft Assessment without Quantitation
8b Internal Agency Review of Draft Assessment
8 Develop Draft Assessment; with both qualitative and quantitative chapters; addressing public and Interagency comments on previous draft
7 Development of New Studies; design and implement research to close data gaps
6 Interagency Evaluation to Close Data Gaps for Mission Critical Chemicalsjamelle96
4e Federal Agencies Identify Mission Critical Chemicals; based on Draft Qualitative Assessment, decision to develop new data, 18 months; if no new studies then go to Step 14
4g Public Listening Session for comment on Qualitative Draft; announced in FRN in Step 10a
4a Public Release of the Draft Qualitative Assessment; for public and Interagency review and comment, announced in FR
3f Internal Agency Review of Draft Qualitative Assessment
9 OMB/Interagency Review of Draft Assessment and Peer Review Charge; multiple reviews
10a Independent Expert Peer Review and Public Comment; public comment period and public peer review workshop announced in FR
10c Public Listening Session for comment on Draft Assessment; announced in FRN in Step 17a
11 Revised Assessment; Post Peer Review; address peer review and public comments
11c Revised Assessment and Disposition of Comments document provided to peer reviewers for review
12a OMB/Interagency Review and Approval; multiple reviews
If significant issue unresolved, then raised to Agency's senior management
12c Internal Agency Review of Final Assessment
12e Revised Assessment; addresses OMB/Interagency comment
13a Final EPA Clearance
13b Post Final Assessment on IRIS


Assessment Development Process for New IRIS
Comprehensive Literature Search and Data Call-In
Completed lit searches posted on Web and announced in FRN
FRN requesting information about studies not in lit search and new research
1 Complete Draft IRIS Assessment
2 Internal Agency Review
3 Science Consultation on the Draft Assessment with other Federal Agencies and White House Offices
EPA coordinates Interagency review
4 Independent Expert Peer Review, Public Review and Comment, and Public Listening Session
Draft assessment and peer review charge posted on Web site
Public comment period and Listening Session announced in FRN
Peer review meeting announced in FRN
5 Revise Assessment
Address peer review and public comments; prepare response to comments document
6A Internal Agency Review and EPA Clearance of Final Assessment
6B EPA-led Interagency Science Discussion
Science feedback on final assessment from other Federal Agencies and White House offices
7 Post Final Assessment on IRIS
Includes IRIS summary, Toxicological Review and response to comments

Appendix C[23]

EPA United States Environmental Protection Agency

Recently Completed Health Assessments

FY2009

- Nitrobenzene
- Cerium
- Chlordecone
- 2-hexanone
- 1,2,3-trichloropropane
- Thallium

FY2010

- Acrylamide
- Carbon tetrachloride
- EGBE
- 1,4-dioxane
- Hydrogen cyanide
- Cis- and trans-1,2-dichloroethylene
- 1,1,2,2-tetrachloroethane
- Pentachlorophenol
- Chloroprene

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[23] NCEA IRIS document, *supra*, note 4

Appendix D[24]

Active Chemicals on the IRIS Agenda

- Acetaldehyde
- Acrylonitrile
- Arsenic (cancer)
- Arsenic (noncancer)
- Asbestos (Libby)
- BBP
- Benzo[a]pyrene
- Beryllium (cancer)
- Biphenyl
- N-butanol
- T-butanol
- Cadmium
- Chloroform
- Chromium VI
- Cobalt
- Copper
- DEHA
- DEHP
- Dibutyl phthalate
- 1,2-, 1,3-, 1,4-dichlorobenzenes
- Dichloromethane
- Disobutyl phthalate
- Disononyl phthalate
- Diethyl phthalate
- 1,4 dioxane (inhalation)
- Dioxin
- Dipentyl phthalate
- ETBE
- Ethylene oxide (cancer)
- Formaldehyde
- Hexabromocyclododecane
- Hexachlorobutadiene
- Hexachloroethane
- Methanol
- Mirex
- MTBE
- Naphthalene
- Nickel
- PAH mixtures
- PCBs (noncancer)
- Phthalate cumulative assessment
- Platinum
- RDX
- Tetrachloroethylene
- Tetrahydrofuran
- Trichloroacetic acid
- Trichloroethylene
- 1,2,4- and 1,3,5-trimethylbenzene
- Uranium
- Urea
- Vanadium pentoxide
- Vinyl acetate

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[24] Ibid.

Appendix E[25]

EPA United States Environmental Protection Agency

Selected Major Upcoming Assessment Products

Chemical	Step in IRIS Process	Target Date for Posting
Arsenic (cancer)	Focused 2nd external peer review (SAB) report received Feb 2011	Aug 2011
Chromium VI	External peer review (independent panel meets May 2011	Sep 2011
Dioxin	External peer review (SAB)	Dec 2011
Formaldehyde	External peer review (NAS)	TBD
Halogenated Platinum Salts	Agency/interagency review	Sep 2011
Libby amphibole asbestos	Agency review	Sep 2012
PCBs (noncancer)	Draft development	Sep 2012
Phthalates cumulative assessment	Draft development	Sep 2012
Polycyclic aromatic hydrocarbon (PAH) mixtures	External peer review (SAB) report received Mar 2011	Dec 2011
Tetrachloroethylene (perc)	External peer review (NAS)	Jul 2011
Trichloroethylene (TCE)	External peer review (SAB)	Sep 2011

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[25] Ibid.

Appendix F[26]

Key Terms

- Reference Concentration (RfC): an **estimate of a continuous inhalation exposure to the human population** (including sensitive subgroups) that is **likely to be without an appreciable risk of deleterious effects during a lifetime**. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

- Reference Dose (RfD): An **estimate of a daily oral exposure to the human population** (including sensitive subgroups) that is **likely to be without an appreciable risk of deleterious effects during a lifetime**. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

- Inhalation Unit Risk (IUR): **The upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 µg/m^3 in air.** The interpretation of inhalation unit risk would be as follows: if unit risk = 2 × 10^{-6} per µg/m^3, 2 excess cancer cases (upper bound estimate) are expected to develop per 1,000,000 people if exposed daily for a lifetime to 1 µg of the chemical per m^3 of air.

- Oral slope factor (OSF): **An upper bound, approximating a 95% confidence limit, on the increased cancer risk from a lifetime oral exposure to an agent**. This estimate is generally reserved for use in the low-dose region of the dose-response relationship, that is, for exposures corresponding to risks less than 1 in 100.

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[26] Ibid.