UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

APR 10 2008

DEPUTY ADMINISTRATOR

MEMORANDUM

FROM: Marcus Peacock

TO: George Gray
Assistant Administrator, ORD

SUBJECT: Implementation of Revised IRIS Process

I understand that the Agency has completed its review of the IRIS process. The revised process is described in the document entitled "*EPA's Integrated Risk Information System: Assessment Development Procedures*" (attached). As you are aware, reforming the IRIS process has been an important goal of the Administrator, as reflected in his Action Plan.

I believe that the revised IRIS process will provide greater transparency, objectivity, balance, rigor and predictability in IRIS assessments. For example, the revised process creates a new step that allows the public to bring forth additional scientific information and to comment on the scope of an assessment early in the IRIS process. New opportunities are also provided for EPA to host a "listening session" during public review and comment periods to allow for broader participation and engagement of interested parties. Additionally, the revised process creates a limited opportunity for other agencies to collect data to fill significant data gaps for "mission critical" chemicals. Although interagency comments on IRIS assessments are considered deliberative in nature (as is the case for all EPA assessments), all conclusions reached by the Agency, including justifications for making science or science policy decisions, are made available to interested parties and the public in the assessment and all IRIS assessments undergo a thorough peer review. Final decisions on the content of IRIS assessments clearly remain with EPA.

These and other improvements to the IRIS process help to define critical and appropriate roles for public and interagency comments and interactions, and promote and foster greater communication and sharing of information between interested parties and EPA. I believe that the outcome of these improvements will be a more predictable, streamlined, and transparent process for conducting IRIS assessments, which will ultimately lead to assessments that are of the highest quality and rigor. The revised process is also expected to result in a much more timely completion of IRIS assessments than has occurred in the past.

The Administrator gave us this task three years ago. Given this and the many advantages the revised process holds relative to past or current practices, the Agency should begin following the steps outlined here as soon as possible. Consequently, I request that you implement the new

IRIS process in all ongoing and future scientific and science-policy assessments, effective immediately. This process, however, should be seen as a "living" document that can be revised and improved as experience is gained and new ideas brought forward. I encourage you to share this process widely and encourage review and comment from interested parties.

The revised IRIS process will yield assessments that are of the highest quality and timeliness, so that they can be used by the Agency, States, the public and various other stakeholders. I look forward to continuing to work with you to advance the Agency's goals through this important process.

Attachment

EPA's Integrated Risk Information System

Assessment Development Procedures

Introduction: The Integrated Risk Information System (IRIS) is a U. S. Environmental Protection Agency (EPA) database that contains the Agency's science and science policy positions on chronic human health effects that may result from exposure to environment contaminants. Through IRIS, EPA provides the highest quality science-based human health assessments to support Agency policymaking activities.

Since the 1980s when IRIS began, EPA has taken many steps to improve the IRIS process that make it more accessible and transparent. In addition, the Agency has worked to enhance the independent expert peer review process to assure high quality human health assessments. In its continuing efforts to improve risk assessment practices, EPA has reviewed its development processes for human health assessments that, once completed, are included on IRIS.

The role of other Federal agencies and the public in the IRIS process is to promote communication, sharing of information, and teaming with EPA at key points throughout the nomination and assessment activities. Agencies may identify chemical substances that are critical to their mission and operation, therefore initiating targeted discussions with EPA in the development of risk assessments for these mission critical chemicals. The public is also offered opportunities to bring forth data and expertise to inform the IRIS process. The enhanced transparency brought about by teaming of other Federal agencies and the public with EPA will help identify scientific issues early, which will ultimately help streamline the IRIS process.

I. Annual Chemical Nomination Process

1. EPA Initiates Annual Nomination Process for IRIS Assessments (75 days)

A. EPA's Office of Research and Development (ORD) issues a *Federal Register* (FR) notice inviting public nominations of chemical substances for ORD to consider for inclusion on the IRIS Program annual agenda (Agenda). Nominations could include chemical substances to consider for the development of new assessments as well as the revision of assessments already on IRIS for which critical new information is available. Nominations must be submitted within 60 days of the solicitation.

B. Simultaneously, ORD asks the EPA Program and Regional Offices and other agencies to nominate chemical substance(s) for inclusion on the Agenda.

   a. Agencies include, but are not limited to, HHS, NASA, DOA, DOE, DOT, DOD, OMB, CEQ, and OSTP.

   b. Each interested agency appoints one point of contact (POC) at the organizational level it deems appropriate. Each agency POC is responsible for keeping their management appropriately informed and for coordinating reviews of draft IRIS documents by that agency.

   c. ORD appoints the POC in the IRIS program.

   d. ORD notifies EPA Program and Regional Offices via memorandum to the EPA Deputy Assistant Administrators and Deputy Regional Administrators, with a copy to the intra-Agency IRIS Review Committee (via email), about the request for assessment nominations.

e. ORD notifies the other agencies via memorandum to the agency POCs (via email) about the request for assessment.

f. Other agencies and EPA Program and Regional Offices have 60 days to submit nominations for inclusion on the Agenda; nomination submittals will be considered part of the public record.

g. If an other agency or EPA Program and Regional Office does not respond within 60 days of the solicitation ORD will assume that it did not have any nominations for that year.

h. Other agencies and EPA Program and Regional Offices provide documentation that supports their interest in the chemical(s) and rationale for consideration to ORD.

C. At the end of the nomination period, within 15 days, ORD calls a meeting with other agencies and EPA Program and Regional Offices to discuss their nominations, including:

a. Other agencies' or EPA's Program and Regional Offices' specific questions and concerns about, and recommendations for, adding or updating assessments for the chemical substance(s) that they nominate;

b. The importance that other agencies or EPA Program and Regional Offices place on having the chemical substance(s) that they nominate included on the Agenda, and the basis for the nomination; and

c. Current or planned research and/or assessments by EPA or the other agencies.

2. EPA Determines Annual IRIS Agenda (30 – 60 days)

A. ORD applies its published selection criteria to the slate of nominated chemicals.

B. ORD reviews its available work force and areas of expertise that might be available for new assignments.

C. ORD prepares the IRIS Program Annual Agenda, which lists the chemical substances for which work will be initiated in the upcoming year, including chemicals selected by ORD and consideration of chemicals nominated in response to **Step 1.A** and **Step 1.B**.

D. ORD notifies EPA Program and Regional Offices, other agencies, and the public that the IRIS Program Annual Agenda is available.

a. Notify EPA Program and Regional Offices by memorandum to the EPA Deputy Assistant Administrators and Deputy Regional Administrators, with a copy to the intra-Agency IRIS Review Committee (via email).

b. Notify other agencies by memorandum to agency POCs (via email).

c. Notify public by issuing an FR notice announcing the IRIS Program Annual Agenda (new starts and updates).

E. The other agencies or EPA Program and Regional Offices may decide at this early stage to sponsor or perform research associated with the chemicals selected or proposed to be assessed if they conclude that such work would be beneficial to the assessment or future re-assessments. The results of this research will be considered for inclusion in the IRIS assessment if it is completed within an appropriate time frame as determined by ORD and has undergone independent external peer review (e.g., peer review publications or independent peer review panel evaluations).

F. The other agencies identify to ORD an initial list of the chemical(s) on the IRIS Program Annual Agenda that they have determined meet the definition of mission critical [1].

II. The Assessment Process

1. EPA Conducts Scientific Literature Search (60 – 90 days)

A. ORD appoints a chemical manager(s) for each chemical on the IRIS Program Annual Agenda.

B. The chemical manager(s) direct an EPA contractor to conduct and complete a comprehensive search of the scientific literature for the chemical.

2. EPA Initiates Data Call-In (45 – 60 days)

A. After the literature search has been completed for each chemical, ORD publishes an FR notice that notifies the public that completed literature searches for a set of chemicals are available on the IRIS Internet site, and invites the public and other agencies to submit additional scientific information (studies, reports, other assessments, etc.) on the chemical.

   a. FR notice requests information on new research that may be planned, underway, or in press.

   b. FR notice includes notification that the initial literature review results for each chemical are available on the Internet for review (eliminates submission of information about which EPA is already aware).

   c. FR notice includes information on how and where to submit scientific information.

   d. A minimum of 45 days is provided for submission of information.

B. ORD ensures that EPA Program and Regional Offices and other agencies are aware of the FR notice:

   a. EPA Program and Regional Offices: via email

   b. Other agencies: via email to agency POCs. Each agency POC is responsible for keeping his/her management appropriately informed.

C. Other agencies confirm to ORD whether the chemical is mission critical. It is expected that only a few chemicals will receive this designation.

[1] A mission critical chemical is one that is an integral component to the successful and safe conduct of an Agency's mission in any or all phases of its operations. Impacts on use of mission critical chemicals include cessation or degradation of the conduct of the mission and/or unacceptable resource constraints.

3. EPA Begins IRIS Assessment and Develops Draft Qualitative Assessment (180 – 240 days)

A. ORD identifies and assembles an IRIS assessment team.

B. ORD reviews new scientific information submitted in response to the call for information in **Step 2.**

C. ORD assesses the data in the scientific literature and submitted in **Step 2** and develops a draft Qualitative Assessment for the chemical being assessed, including:

   a. summary of potentially important health effects;

   b. summary of information on potential mode(s) of action;

   c. summary of information about potentially susceptible populations;

   d. description of approaches being considered for dose-response assessment including default approaches and types of models under consideration;

   e. identification and discussion of potential uncertainty factors; and

   f. identification of potential uncertainties that impact the qualitative and quantitative aspects of the assessment.

D. This draft Qualitative Assessment does not include quantification; however, extensive qualitative information including ORD's interpretation of scientific data and description of potential assumptions and approaches will be included.

E. The draft Qualitative Assessment completes internal ORD clearance.

F. The draft Qualitative Assessment completes internal EPA review via the intra-Agency IRIS Review Committee. Intra-Agency comments are deliberative.

4. EPA Initiates Public and Agency Review of Draft Qualitative Assessment (45 – 60 days)

A. ORD issues a FR notice inviting the public and other agencies to comment on the draft Qualitative Assessment.

B. On the publication date of the FR notice, the draft Qualitative Assessment is posted on the IRIS Internet site.

C. ORD ensures that EPA Program and Regional Offices and other agencies are aware of the FR notice.

D. The FR notice includes instructions for submitting comments to ORD. The FR notice also requests that the public and other agencies identify missing types of studies and areas where uncertainties might be reduced, modes of action elucidated, or estimation of dose-response informed through new short-term (12 month) research.

E. Other agencies may identify a chemical as mission critical based on the results of the draft Qualitative Assessment (see Annual Chemical Nomination Process - **Step 2.F)**.

F. All public comments received during the official public comment period must be submitted through E-Gov (www.regulations.gov); all public comments will be part of the official record. Other agency comments are deliberative.

G. ORD holds a "listening session" during the public review process to allow all interested parties to comment on the draft Qualitative Assessment.

5. EPA Initiates Review of Public and Agency Comments (30 days)

A. ORD compiles and reviews all public and other agency comments received on the draft Qualitative Assessment, and shares the comments with EPA Program and Regional Offices and other agencies.

B. ORD provides other agencies and EPA Program and Regional Offices with information about any significant changes that might occur in the IRIS assessment as a result of the public or other agency comments and listening session.

C. If another agency or the public wants to discuss with ORD a particular comment or set of comments, they should contact the IRIS POC to arrange a meeting with ORD.

D. If significant alternative science or science policy judgments are raised by the public, EPA Program or Regional Offices, or other agencies, these will be added to the document and brought forward in the charge to the independent external peer review panel.

6. Evaluation of Agency Interest in Closing Data Gaps for Mission Critical Chemicals (90 days)

A. If another agency is interested in filling a significant data gap, it must first document that the chemical is mission critical (see Annual Chemical Nomination Process - **Step 2.F** and The Assessment Process - **Step 4.E**).

B. For mission critical chemicals, the agency interested in addressing data gaps will consider the comments provided in **Steps 4 and 5**, and submit to ORD a research plan that documents how the conduct of new research has the potential to reduce uncertainties, clarify the mode-of-action, or inform the estimation of dose-response. The other agency must also show that the proposed research and peer review can be completed in less than 18 months. If desired, a letter of agreement between ORD and the other agency sponsoring the research can be created articulating the relevance of the proposed research to the risk assessment and how the proposed research may inform the risk assessment. Such a letter would indicate the timeframe for expected research to be completed.

C. The sponsoring agency may decide that an independent 3rd party consultation should be done to evaluate the estimated costs of the proposed research, and the expected benefits of additional research for the assessment. This 3rd party consultation must be completed during this 90 day period.

D. If a sponsoring agency wants to partner with an external party or any other agency to conduct a study, that decision is theirs to make, but ORD and other interested agencies should be informed.

E. If no request for developing new short-term research is received, or if no interest in conducting such research is expressed for mission critical chemicals, proceed to **Step 8.**

7. Design and Implementation of New Studies for Mission Critical Chemicals (365 – 540 Days)

A. If in **Step 6** the consequences and interest in closing data gaps are determined to be critical by ORD, in consultation with the intra-Agency IRIS Review Committee and other interested agencies, the agency can sponsor the new research.

B. ORD will generally allow no more than an 18 month hiatus from the completion of the IRIS assessment to allow for the completion and peer review of studies specified in **Step 6**.

C. The sponsoring agency develops a detailed research plan and solicits comments and recommendations on the research plan from ORD, in consultation with the intra-Agency IRIS Review Committee, and from other agencies. ORD and the other agencies respond to the sponsoring agency within 30 days, focusing on study design and whether the research, if conducted as planned, is likely to reduce uncertainties (e.g., specific uncertainty factor), clarify the mode-of-action, or inform the estimation of dose-response. The study plan and characterization of potential impacts on the assessment is documented in a letter between the sponsoring agency and ORD, as a complement to the letter discussed in **Step 6.B**.

D. The agency sponsoring the research will work expeditiously to complete its planning, protocol design, and study implementation. ORD, in consultation with the intra-Agency IRIS Review Committee, will provide timely reviews and responses of any aspect of this work, if requested by the sponsoring agency.

E. If ORD or the sponsoring agency deems that consultations are warranted, ORD or the sponsoring agency can call meetings and teleconferences to discuss critical issues articulated in correspondence among the agencies. Third-party consultants can be invited by ORD or the other agencies to participate in these meetings and teleconferences.

F. An agency may also sponsor or perform any other research (that is outside the scope of this effort) associated with the chemical being assessed if it concludes that such work might be beneficial to a future IRIS assessment. Agencies will continue to direct their internal research agendas as they see fit.

G. The sponsoring agency provides the study report(s) to ORD and other interested agencies immediately upon completion of the study.

H. Independent External Peer Review (included as part of **Step 7** timeframe):

   a. Upon completion of the study, the sponsoring agency arranges for external peer review of the research report(s) by the scientific community.

   b. The sponsoring agency consults with ORD in determining who will conduct this review, the level of review, and by what means (e.g., panel review).

   c. ORD and the sponsoring Agency provide the studies, peer review comments and disposition of comments report(s) to the public.

   d. If ORD or the sponsoring agency deems that consultation is warranted, ORD or the sponsoring agency may call a meeting to discuss critical issues and significant disagreements about the peer reviews. Third-party consultants may be invited by ORD or the sponsoring agency to participate in this meeting.

I. ORD, in consultation with the intra-Agency IRIS Review Committee, will consider the results of the new studies carefully as it proceeds with the development of the assessment. Discussion of the new study results will be included in the draft assessment.

8. EPA Completes Draft IRIS Toxicological Review (120 – 270 days)

A. ORD completes the draft IRIS Toxicological Review.

a. The draft IRIS Toxicological Review draws upon the previous draft Qualitative Assessment and the comments received in **Steps 4 and 5.**

b. ORD reviews and analyzes any new short-term research completed under **Steps 6 and 7.**

c. The draft IRIS Toxicological Review includes a quantitative assessment, including application of uncertainty factors, mode-of-action information, and dose-response modeling.

B. The draft IRIS Toxicological Review undergoes internal ORD review (30 – 45 days).

C. ORD submits the draft IRIS Toxicological Review for internal review via the intra-Agency IRIS Review Committee and addresses intra-Agency comments (30 – 60 days).

D. Determination of peer review characteristics:

a. For mission critical chemicals, ORD will cooperate with other interested agencies to determine the level of peer review (e.g., National Academy of Science (NAS) review, EPA Science Advisory Board (SAB) review, or contractor-led panel peer review), panel disciplines, and the scope of the review.

b. For other chemicals, ORD determines the level of peer review, panel disciplines, and the scope of the review.

c. ORD develops any contract documentation.

9. EPA Initiates Interagency Review of Draft IRIS Toxicological Review (45 – 105 days)

A. ORD sends the draft IRIS Toxicological Review and draft external peer review charge questions to OMB to initiate interagency review.

B. ORD develops a charge for interagency reviewers. It is anticipated that the interagency review charge will remain similar for each draft IRIS Toxicological Review, with chemical specific text added as appropriate.

C. OMB distributes the draft IRIS Toxicological Review, draft external peer review charge questions, and the interagency review charge to interagency reviewers.

a. Length of review period is 30 – 60 days and depends on complexity of draft assessment documents.

b. OMB facilitates interagency review to help assure timely response within designated review period.

D. OMB compiles and provides all interagency comments to ORD; other agency comments are deliberative.

a. ORD assumes “no comment” from other agencies that do not respond within the designated review period.

b. If another agency requests an extension of the review period, both the IRIS POC and OMB POC should be contacted regarding the request and the justification.

E. ORD addresses the interagency comments and develops a “disposition of comments” document and revises the draft assessment documents, as appropriate, within 15 – 30 days.

F. Within 15 days after the comment period ends, ORD, OMB, or other interested agencies may call a meeting to discuss and resolve critical issues and significant disagreements articulated in the other agencies' comments on the draft assessment documents.

   a. OMB serves as the facilitator for the meeting.

   b. Areas of disagreement may result in additional charge questions for the external peer review.

10. EPA Initiates Independent External Peer Review and Releases External Draft IRIS Toxicological Review (120 – 280 days[2])

A. ORD provides the draft IRIS Toxicological Review and peer review charge questions to independent external peer reviewers. Peer reviews are public meetings, generally through a face-to-face meeting of panelists, though some may be held via public teleconference.

B. Concurrently, ORD publicly releases the draft IRIS Toxicological Review and charge to peer reviewers for public review and comment on the IRIS Internet site.

   a. ORD prepares an FR notice announcing a public comment period of 45 to 60 days.

   b. Length of the public comment period depends on the complexity of the draft IRIS Toxicological Review.

   c. The draft IRIS Toxicological Review and charge to peer reviewers is released on the IRIS Internet site on the day that the FR is published.

   d. Public comment period is open to all stakeholders, including other agencies.

   e. ORD insures that other agencies are aware of the FR notice.

C. ORD holds a "listening session" during the public comment process to allow all interested parties to comment on the draft IRIS Toxicological Review.

D. Public comments from Steps B and C are submitted to ORD.

   a. All public comments received during the official public comment period will be submitted through E-Gov (www.regulations.gov); all public comments will be part of the official record.

   b. Comments received by the close of the public comment period will be provided to the external peer review panel at least 30 days in advance of the peer review meeting.

E. The report of the external peer review panel becomes part of the public record for the IRIS assessment.

11. EPA Revises IRIS Toxicological Review and Develops IRIS Summary (120 – 150 days)

A. ORD evaluates the external peer review panel report and public comments.

B. ORD revises the draft IRIS Toxicological Review, as appropriate, and develops the IRIS Summary.

C. Length of revision process depends on the complexity of the IRIS Toxicological Review and complexity and number of peer reviewer and public comments.

[2] This time frame does not include reviews conducted by the National Academy of Sciences (NAS).

D. Within 90 – 120 days, ORD develops a disposition of peer reviewer and public comments and provides the disposition of comments document and the revised IRIS Toxicological Review and IRIS Summary to the external peer review panel members for their comment within 30 days.

E. ORD provides the disposition of peer reviewer and public comments document and any additional peer review panel comments from **Step 11.D** as an appendix to the IRIS Toxicological Review.

12. EPA Initiates Final Agency and Interagency Review of the IRIS Toxicological Review and IRIS Summary (30 – 45 days)

A. ORD sends the final IRIS Toxicological Review and IRIS Summary to OMB for distribution to the other agencies.

B. In general, this distribution is intended as a final check-in to address any remaining issues and ensure that public and peer reviewer comments were adequately considered or addressed by ORD.

C. Concurrently, ORD sends the IRIS Toxicological Review and IRIS Summary to the intra-Agency IRIS Review Committee for comment (30 days).

D. OMB compiles and provides all interagency comments to ORD within 30 days.

   a. ORD assumes “no comment” if the other agencies or EPA Program or Regional Offices do not respond within the designated review period.

   b. If another agency or EPA Program or Regional Office requests an extension of the review period, both the IRIS POC and OMB POC should be contacted regarding the request and the justification.

E. ORD addresses and resolves any remaining issues in consultation with OMB and other agency or EPA Program or Regional Office POCs within 15 days. Should resolution of any issue not be achieved in discussions with the POC, the other agency or EPA Program or Regional Office that raised the issue may decide to elevate the discussion to their senior management level to achieve resolution. The final decision on IRIS content remains with EPA.

13. EPA Completion of IRIS Toxicological Review and IRIS Summary (60 days)

A. ORD completes the IRIS Toxicological Review and IRIS Summary.

B. ORD prepares the final assessment to post on the IRIS Internet site.

C. ORD insures 508 Compliance and EPA web site compliance.

D. ORD posts the assessment to the IRIS Internet site. ORD completes and maintains the public record.