IRIS

BACKGROUND PAPER

Integrated Risk Information System

Office of Health and Environmental Assessment

Office of Research and Development

FEBRUARY, 1993

VERSION 1.0

IRIS Background Paper

On February 25, 1993, a FEDERAL REGISTER notice (58 FR 11490) was published on the Integrated Risk Information System (IRIS). This background paper is a companion piece to that notice.

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For further information on IRIS, please contact:

IRIS User Support
(Operated by Computer Sciences Corporation)
26 W. Martin Luther King Drive (MS-190)
Cincinnati, OH 45268

Telephone (513) 569-7254 Facsimile (513) 569-7916

Introduction

This background paper provides the of history, purposes, and goals of the Integrated Risk Information System (IRIS) and a detailed description of the current processes used by the two Agency scientific work groups responsible for developing the health hazard information in IRIS. This background will help interested persons to better understand the focus and contents of the companion FEDERAL REGISTER notice.

The February 25, 1993 FEDERAL REGISTER notice (58 FR 11490): (1) announces the availability of this paper that describes IRIS, its contents, and the current processes used by the two Agency work groups responsible for developing IRIS information; (2) discusses an Agency activity to review IRIS processes and solicits comments on this review; (3) highlights points in the current process where public input, including information submissions, is encouraged; (4) describes how to access IRIS; and (5) announces a new process to publish regularly a list of the substances scheduled for IRIS work group review and to solicit pertinent data, studies, and comments on these substances.

General Background

IRIS is an EPA data base, updated monthly, containing Agency consensus positions on the potential adverse human health effects of approximately 500 specific substances. It contains summaries of EPA qualitative and quantitative human health information that support two of the four major steps of the risk assessment process outlined in the National Research Council's (NRC) 1983 publication, "*Risk Assessment in the Federal Government: Managing the Process.*"

The risk assessment process described in the 1983 NRC publication consists of four major steps: hazard identification, dose-response evaluation, exposure assessment, and risk characterization. IRIS includes information in support of the first two of those steps, hazard identification and dose-response evaluation. Hazard identification is the qualitative determination of how likely it is that a substance will increase the incidence and/or severity of an adverse health effect. Dose-response evaluation is the quantitative relationship between the magnitude of the effect and the dose inducing such an effect. IRIS information supporting risk characterization consists of brief statements on the quality of data and very general statements on confidence in the dose-response evaluation. IRIS consensus information does not include exposure assessment information. Combined with specific situational exposure assessment information, the summary health hazard information in IRIS may be used as one source in evaluating potential public health risks of or from environmental contaminants.

Many EPA program offices and program support offices, including the Office of Research and Development, both at Headquarters and in EPA's ten Regional offices, are involved in assessment activities in support of various legislative mandates. In the 1980s, as health risk assessment became a more widespread practice across Agency programs, the need became clear for greater consensus and consistency in the areas of hazard identification and dose-response assessment. It was determined that an internal process should be established for reaching an Agency-wide judgment on the potential health effects of substances of common interest to these offices, and a system developed for communicating that Agency judgment to EPA risk assessors and risk managers. These would provide the needed consistency and coordination. In 1986, two EPA work groups with representation from program offices involved in risk assessment were convened to carry out such an internal process to reach consensus Agency positions on a chemical-by-chemical basis. In 1986, the IRIS data base was created for EPA staff as the official repository of that consensus information.

On June 2, 1988, a FEDERAL REGISTER notice (53 FR 20162-20164) of public availability of IRIS was published. That notice described IRIS, the types of risk information it contains, and how to get access to the system. It informed the public about the establishment of the IRIS Information Submission Desk. The submission desk was intended to provide opportunity for public input. The notice explained the procedures for submission of data or comments by interested parties on substances either on IRIS or scheduled for review by the work groups. As stated in the June 1988 notice, a list of the substances scheduled for work group review has been a separate file on IRIS since it became publicly available. It was hoped that users would submit pertinent information to the IRIS Information Submission Desk. In fact, few users have taken advantage of the opportunity to submit data and comments.

Therefore, data submission procedures are reiterated in the FEDERAL REGISTER notice (58 FR 11490) related to this paper and a list of the substances scheduled for review by specific work groups is included. The data submission procedures will be reprinted in the FEDERAL REGISTER every 6 months with a new or revised list of substances scheduled for work group review. For the latest status of the substances scheduled for review, interested persons should first check the IRIS data base itself or contact:

IRIS User Support (Operated by Computer Sciences Corporation)
U.S. EPA
26 W. Martin Luther King Drive (MS-190)
Cincinnati, OH 45268
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Data Base Contents

The core of IRIS is the three consensus health hazard information summary sections: the reference dose for noncancer health effects resulting from oral exposure, the reference concentration for noncancer health effects resulting from inhalation exposure, and the carcinogen assessment for both oral and inhalation exposure. All of these terms are commonly used for judging the effects of lifetime exposure to a given substance or mixture. Citations for the scientific methodologies that are the basis for the consensus health hazard sections on IRIS are included on page 10 of this paper.

In addition, an IRIS substance file may include supplemental information such as summaries of health advisories, regulatory actions, and physical/chemical properties.

Noncancer Health Effects Information

An oral reference dose (RfD) is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is believed likely to be without an appreciable risk of certain deleterious effects during a lifetime ("Reference Dose [RfD]; Description and Use in Health Risk Assessment" *Regulatory Toxicology and Pharmacology* 8:471-486, 1988). RfDs are developed by an assessment method that assumes that there is a dose threshold below which adverse effects will not occur. An RfD, which is expressed in milligrams per kilogram per day (mg/kg-day), is based on the determination of a critical effect from a review of all toxicity data and a judgment of the necessary uncertainty and modifying factors based on a review of available data. IRIS substance files contain the following information pertaining to the oral RfD: reference dose summary tables, principal and supporting studies, uncertainty and modifying factors used in calculating the RfD, a statement of confidence in the RfD, EPA documentation and review, EPA scientific contacts, and complete bibliographies for references cited.

The inhalation reference concentration (RfC) is analogous to the oral RfD (*Interim Methods for Development of Inhalation Concentrations*, EPA/600/8-90/066A). It is also based on the assumption that thresholds exist for noncancer toxic effects. The RfC considers toxic effects for both the respiratory system (portal-of-entry) and for effects peripheral to the respiratory system (extra-respiratory). The inhalation RfC is expressed in milligrams per cubic meter (mg/cu.m). The RfC method departs from that used to determine the oral RfD primarily by the integration of the anatomical and physiological dynamics of the respiratory system (i.e., portal-of-entry) with the physicochemical properties of the substance or substances entering the system. Different dosimetric adjustments are made according to whether the substance is a particle or gas and whether the observed toxicity is respiratory or extra-respiratory. These adjustments scale the concentration of the substance that causes an observed effect in laboratory animals (or in humans, when available from occupational epidemiology studies) to a human equivalent concentration for ambient exposures.

IRIS substance files contain the following inhalation RfC information: reference concentration summary tables, description of dosimetric adjustment, principal and supporting studies, uncertainty and modifying factors used to calculate the RfC, a statement of confidence in the RfC, EPA documentation and review, EPA scientific contacts, and complete bibliographies for references cited.

Cancer Health Effects Information

The carcinogen assessment of an IRIS substance file contains health hazard identification and dose-response assessments developed from procedures outlined in the EPA Guidelines for Carcinogen Risk Assessment (51 FR 33992-43003, September 24, 1986). Each cancer assessment, as a rule, is based on an Agency document that has received external peer review. The hazard identification involves a judgment in the form of a weight-of-evidence classification of the likelihood that the substance is a human carcinogen. It includes the type of data used as the basis of the classification. This judgment is made independently of considerations of the strength of the possible response. The dose-response assessment is a quantitative estimate of the potential activity or magnitude of a substance's carcinogenic effect, usually expressed as a cancer unit risk. A cancer unit risk is an upper-bound estimate on the increased likelihood that an individual will develop cancer when exposed to a substance over a lifetime at a concentration of either 1 microgram per liter (1 μg/L) in drinking water for oral exposure or 1 microgram per cubic meter (1 μg/cu.m) in air for continuous inhalation exposure. Generally, a slope factor for dietary use is also given. It is an upper-bound estimate of cancer risk for humans per milligram of agent per kilogram of body weight per day.

IRIS contains the following information in the cancer assessment section: EPA weight-of-evidence classification and its basis, a summary of human carcinogenicity studies when available, a summary of animal carcinogenicity studies, a summary of other data supporting the classification, oral and/or inhalation quantitative estimates, dose-response data used to derive these estimates and the method of calculation, statements of confidence in magnitude of unit risk, documentation and review, EPA scientific contacts, and complete bibliographies for references cited.

Scientific Contacts

It is important to note that in each of the three sections described above, EPA staff names and telephone numbers are included as scientific contacts for further information. The Agency believes that the inclusion of Agency scientific contacts able to discuss the basis for the Agency's position, has been very valuable. These individuals play a major role in providing public access to IRIS and a conduit for valued public comment.

Bibliographies

IRIS contains full bibliographic citations for each substance file, directing the user to the primary cited studies and pertinent scientific literature. One of the major intents of IRIS was to encourage users to evaluate the primary literature used to develop the IRIS information in light of the assumptions and uncertainties underlying the risk assessment process.

Supplementary Information

In addition to the RfD, RfC, and carcinogenicity sections, IRIS substance files may contain one or more of three supplementary information sections: a summary of an Office of Water's Drinking Water Health Advisory, a summary of EPA regulatory actions, and a summary of physical/chemical properties. The only purpose of these supplemental sections is to serve as accessory information to the consensus health hazard information. Since the primary intent of the IRIS date base is to communicate EPA consensus health hazard information, these other sections are only included as auxiliary material to provide a broader profile of a substance and are never added until at least one of the consensus health hazard sections described above (namely, the RfD section, RfC section, or carcinogenicity section) is prepared and approved for final inclusion on the data base. These supplemental sections should not be used as the sole or primary source of information on the current status of EPA substance-specific regulations.

Use and Development of Health Hazard Information

The type of substance-specific consensus health hazard information on IRIS may become part of the supporting materials used to develop site-specific EPA health hazard assessments. These assessments may in turn lead to EPA risk management decisions, generally resulting in the formal Agency rulemaking process. This rulemaking process often includes FEDERAL REGISTER publication of a proposed rule where the public is encouraged to comment. These comments may be directed at both the proposed rule and the scientific basis of the decision, including information obtained from IRIS and thus offer a further opportunity for comment on the risk information in the context of its use.

The area of human health risk assessment has evolved over the past several years. As the risk assessment community has grown and the field itself has matured, new approaches to the assessment and use of human health risk information have been developed. The evolving nature of risk assessment has also resulted in changes to IRIS. The development of methodologies such as those for the inhalation RfC determination illustrates the ability of the IRIS information development process to grow with the changing science. Areas of future growth may include less-than-lifetime risk information and developmental toxicity risk information and other endpoint-specific health hazard information. Also, on several occasions, the information in IRIS has

been reevaluated and modified to reflect new information and approaches. New studies on individual substances are continually being conducted by Federal, private, and academic institutions and may have significant impact on IRIS information. In those cases, the IRIS substance information is reevaluated in light of the new data; any changes resulting from that reevaluation are included on the system.

Management of the Data Base

The IRIS data base is managed and maintained by the Office of Health and Environmental Assessment (OHEA), Office of Research and Development (ORD). IRIS is an Agency system primarily funded by OHEA with additional significant support from EPA program offices.

Oversight

Oversight activities for IRIS are conducted by the IRIS Oversight Committee, a subgroup of the Agency's Risk Assessment Council. Committee membership consists of senior Agency risk assessors. The main purpose of the IRIS Oversight Committee is to serve as a forum for discussion and advice on significant scientific or science policy issues involving IRIS. The Council, which is chaired by EPA's Deputy Administrator, receives periodic status reports on IRIS and related work group activities.

Information Development Process

There are two EPA work groups, the Carcinogen Risk Assessment Verification Endeavor (CRAVE) and the Oral Reference Dose/Inhalation Reference Concentration (RfD/RfC) Work Group, that develop consensus health hazard information for IRIS. Each group consists of EPA scientists from a mix of pertinent disciplines and represents intra-Agency membership. The work groups serve as the Agency's final review for EPA risk assessment information. When the work groups reach consensus on the health effects information and the dose-response assessment for a particular substance, the descriptive summary is added to IRIS.

CRAVE: Information Development Procedures

The goals of the CRAVE are to reach Agency consensus on Agency carcinogen risk assessments; to arrive at a unified view on potential cancer risk from exposure to specific substances across Agency programs; and to identify, discuss, and resolve general issues associated with methods used to estimate carcinogenic risks for specific agents. The major outputs of the work group are summaries of risk

information that have been previously developed and documented by scientific experts in Agency program and program support offices, and results of discussions of general issues in carcinogen risk assessment.

Scientists are selected by executive appointment from respective member offices. Membership is open to all major Agency program and regional offices, ORD, and the Office of Policy, Planning, and Evaluation (OPPE). Substances are discussed at the request of Agency offices or regions according to an established timetable. The CRAVE priorities are determined by the member offices. The office requesting review prepares a summary describing both a judgment on the weight-of-evidence for potential health hazard effects and any dose-response information for the substances according to an established format. Literature files on the substances including critical studies, pertinent EPA documents, and other relevant supporting documentation are made available to work group members in advance of the meeting. Generally, the judgment and the dose-response assessment are expected to have appeared in a publicly available document of some sort.

The CRAVE usually meets bimonthly for two days. Work group members normally receive draft summaries for pre-meeting review at least one week prior to the scheduled meeting. At the meeting, data and documentation are examined, and there is discussion of the basis for the risk information and the methods by which it was derived. In addition, the nature and extent of previous internal and external peer review, including the comments received, are reviewed by the work group. The summary is revised by the office originating the review to reflect the meeting discussion and accurately express the consensus view of the work group. After the process of revision is completed, the summary is circulated again to the work group for final approval prior to its inclusion on IRIS.

Consensus means that no member office is aware either of information that would conflict with the final carcinogenicity summary, or of analyses that would suggest that a different view is more credible. Such assurance rests on the capabilities of the individuals who represent their offices; thus, every effort is made to seek scientists who are both expert in the area of human health assessment and who can represent their office.

Peer review has generally been part of the IRIS information development processes from the beginning of the system. In the preparation of summaries, emphasis has been placed on the use of peer-reviewed EPA assessments. These have included Office of Pesticide Programs assessments that have received both program office peer review and Science Advisory Panel review. Other EPA documentation includes assessments prepared by OHEA such as Health Assessment Documents, Health and Environmental Effects Documents, and Health Effects Assessments. These documents receive OHEA review and program office review and some receive Science Advisory Board (SAB) or other external review. Assessments developed by or for the Office of Ground Water and Drinking Water and incorporated

in either Drinking Water or Ambient Water Criteria Documents, or in Drinking Water Health Advisories generally receive extensive Agency review and SAB review prior to discussion by CRAVE.

On occasion, risk assessments that were contained in draft documents have been discussed by CRAVE. In these instances, results of the work group deliberations have been incorporated into the document development process at the program office or program support office level. Loading of the information on IRIS is delayed pending completion of the document.

If consensus is not reached at the meeting it is generally because an issue is raised that requires resolution. Work group deliberations continue until consensus is achieved. In the case of substance-specific issues, the substance is referred back to the member office that initiated the review for more information and clarification. In some instances, it has been necessary for more than one program office to engage in a dialogue to resolve the issue.

For general issues, CRAVE practice has been to form a subcommittee to prepare an issue paper that is subsequently discussed at a special meeting. As examples of this process, issue papers have been developed for (1) issues relating to accuracy and precision of quantitative dose-response information, (2) factors involving confidence in quantitative estimates, and (3) use of split classifications and combining estimates.

When consensus is not achieved on a particular substance at a meeting of the CRAVE, it is considered to have "under review" status. If after three months, there is no further activity to bring the substance back to the work group for additional review, the substance loses its "under review" status. The substance is then dropped from the work group review list after notifying the responsible office. Any office may resubmit the substance for further discussion at any time.

Reference Dose (RfD)/Reference Concentration (RfC): Information Development Procedures

The purpose of the RfD/RfC Work Group is to reach consensus on oral RfDs and inhalation RfCs for noncancer chronic human health effects developed by or in support of program offices and the regions. The work group also works to resolve inconsistent RfDs or RfCs among program offices and to identify, discuss, and resolve generic issues associated with methods used to estimate RfDs and RfCs.

Scientists are selected by executive appointment from respective member offices. Membership is open to all major Agency program and regional offices. There are two work group co-chairs. In addition, scientists from the Agency for Toxic Substances and Disease Registry and the Food and Drug Administration are invited to work group meetings as observers to assist the Agency in the information gathering process. Their

involvement fosters better communication and coordination among federal agencies regarding assessment approaches and data evaluation. Members reflect a variety of pertinent scientific disciplines including expertise in the fields of general and inhalation human toxicology.

Member offices schedule substances for discussion through the work group co-chairs for specific meetings, usually one or two months in advance. Regional requests for specific substance discussions are routed through the co-chairs, who then either schedule these substances in the usual manner or, if the region has not prepared a file, requests an appropriate office to undertake that task.

The RfD/RfC Work Group usually meets once a month for two days. Substances are discussed at the request of any Agency office or region. The requesting office generally prepares a file that consists of a summary sheet, a copy of the critical study and supporting documentation, and distributes these to work group members prior to the meeting.

Consensus generally means that no member office is aware either of information that would conflict with the RfD or RfC, or of analyses that would suggest a different value that is more credible. Such assurance rests on the capabilities of the individuals who represent their offices; thus, a large effort is conducted biannually to seek scientists who are both expert in this area of assessment and can represent their offices.

RfD or RfC summaries are not always based on existing EPA assessment documents but may be based on assessments prepared specifically for the work group. This is a fundamental difference between the usual processes of the RfD/RfC Work Group and those of CRAVE. As stated previously, the general rule has been that for a substance to be brought to the CRAVE Work Group for review there should be an existing peer-reviewed Agency health effects document. However, for RfDs there may or may not be an existing EPA document on which to base work group deliberations and in the case of RfCs, there have not, to date, been any existing peer-reviewed EPA documents. Thus, RfC deliberations are based on extensive assessment summaries prepared expressly for the work group. Therefore, when an Agency peer-reviewed document is not available, as with RfCs and some RfDs, extensive assessment summaries are included on IRIS once the work group has completed verification and reached consensus.

The work group co-chairs assure that the final summary accurately expresses the consensus view of the group at the meeting as specified in the meeting notes. Once unanimous consensus is reached, the substance-specific summary for either an RfD or RfC is prepared for inclusion on IRIS. In some cases, the work group agrees that adequate information is not available to derive an RfD or RfC. A message is then put on IRIS to that effect and the reasons for the "not verifiable" status. In most cases the message states that the health effects data for a specific substance were reviewed by the work group and determined to be inadequate for derivation of an RfD or RfC.

Conflicts that arise during a meeting regarding a given RfD or RfC generally are resolved outside the meeting by scientists from the appropriate offices, and then brought back to the work group for clarification and subsequent consensus. Conflicts that arise regarding the methods by which RfDs or RfCs are estimated, or the incorporation of new methods, are generally taken up at separately scheduled meetings of the work group, for which the sponsoring office prepares the appropriate material for review.

While, as discussed above, the RfD/RfC Work Group process is somewhat different from that of the CRAVE, they both use generally the same consensus procedures. Other procedural similarities are discussed in the following paragraphs.

On occasion, scientific issues on individual substances, methods, or on a general question cannot be resolved at the work group level. In the event that an issue is unresolvable in the work group processes, the issue is referred to the Risk Assessment Council. In some cases, the issue is brought to the IRIS Oversight Subcommittee for review and discussion, prior to consideration by the full Council. If an issue is raised to the Council, it may be referred by the Council to the Risk Assessment Forum for consultation.

Both the CRAVE and RfD/RfC Work Groups, through the IRIS Information Submission Desk, discussed in the companion FEDERAL REGISTER notice, have received comments and studies from interested parties outside of the Agency that were either pertinent to the work group's initial review or resulted in reconsideration of a particular substance assessment. Further, the work groups often contact the authors of a primary study if clarifications are necessary, and consult with outside experts on scientific issues that require expertise that is not present in the work group. Also, through professional societies and other private sector organizations, the work groups have fostered discussions and exchanges regarding new and innovative approaches to human health assessment methodologies.

Methods and Guidelines

Both Agency work groups responsible for the development of the health hazard information on IRIS use Agency scientific methods documents and EPA's risk assessment guidelines as the basis for their work. These guidelines and methodologies used to develop the RfD or RfC have been peer reviewed by the SAB.

Summaries of methods used for development of oral RfDs and carcinogenicity information on IRIS are contained in IRIS background documents that are available on the system. A paper copy of the oral RfD and CRAVE background documents, "Reference Dose (RfD); Description and Use in Health Risk Assessment" (*Regulatory Toxicology and Pharmacology* 8:471-486, 1988) and *The U.S. EPA Approach for Assessing the Risks Associated with Chronic Exposures to Carcinogens*, respectively, is also available from IRIS User Support by calling: (513) 569-7254.

The draft methods document, *Interim Methods for Development of Inhalation Concentrations* (EPA/600/8-90/066A), is the basis for the inhalation RfCs. A copy of the document is available from the Center for Environmental Research Information (CERI) by calling: (513) 569-7562. Please cite the EPA document number (EPA/600/8-90/066A) when requesting a copy. A revised RfC methodology document based on SAB peer-review comments will undergo a second SAB review and will be available later this year.

The CRAVE background document is based on EPA's 1986 Guidelines for Carcinogen Risk Assessment (51 FR 33992-34003). A copy of the EPA risk assessment guidelines (EPA/600/8-87/045) is also available by calling CERI.

Public Involvement

The section in the companion FEDERAL REGISTER notice (February 25, 1993, 58 FR 11490) on **Current Opportunities for Public Involvement in the IRIS Process** elaborates on opportunities for public input and dialogue.

Federal Register Notice

federal register

Thursday
February 25, 1993

Part III

Environmental Protection Agency

Integrated Risk Information System; Announcement of Availability of Background Paper; Notice

ENVIRONMENTAL PROTECTION

[FRL–4560–8]

Integrated Risk Information System (IRIS); Announcement of Availability of Background Paper

AGENCY: U.S. Environmental Protection Agency.

ACTION: Notice; announcement of availability of background paper on IRIS, request for comments on internal review, and announcement of substances scheduled for work group review.

SUMMARY: The Integrated Risk Information System (IRIS) is a data base of the United States Environmental Protection Agency (EPA) that contains EPA scientific consensus positions on potential human health effects from environmental contaminants. This notice provides information and requests information on IRIS for the purposes of improving the system and addressing questions regarding increased peer review and public participation.

This notice contains three components. First, it announces the availability of a background paper describing IRIS, its contents, and the current processes used by the two Agency work groups responsible for developing the IRIS information. Second, it discusses an Agency activity to review IRIS processes, solicits comments on this activity, and highlights points in the current process where public input is encouraged. Third, it announces a new process for publication of a list of the substances scheduled for IRIS work group review and the solicitation of pertinent data, studies, and comments on these substances. This list will appear in the **Federal Register** every six months for the next six-month period following its publication. The list for March 1 to December 31, 1993, is provided in this notice. Subsequent lists will cover a six-month period.

DATES: Please submit written comments by April 12, 1993.

ADDRESSES: Please send comments, an original and one unbound copy, to: Iris Quality Action Team, Attention: Linda C. Tuxen, Room 3809H, Waterside Mall (RD–689), USEPA, 401 M Street, SW., Washington, DC 20460.

For a copy of the IRIS Background Paper contact: IRIS User Support (Staffed by Computer Sciences Corporation), USEPA, Environmental Criteria and Assessment Office (MS–190), 26 W. Martin Luther King Drive, Cincinnati, OH 45268, Telephone: (513) 569–7254 Facsimile: (513) 569–7916.

FOR FURTHER INFORMATION CONTACT: Linda C. Tuxen, EPA IRIS Coordinator, Office of Health and Environmental Assessment (RD–689), USEPA, 401 M Street, SW., Washington, DC 20460, Telephone: (202) 260–5949 Facsimile: (202) 260–0393.

SUPPLEMENTARY INFORMATION:

Background

IRIS is an EPA data base, updated monthly, containing Agency consensus scientific positions on potential adverse human health effects that may result from exposure to environmental contaminants. Currently IRIS contains health effects information on approximately 500 specific substances.

Since IRIS was developed in 1986 and made available to the public in 1988, its use by EPA and by the environmental health community has grown substantially. EPA uses the data base to provide consistent risk information across EPA programs and the regions. States, national and international organizations, and other public and private organizations involved with assessing potential health hazards of exposure to a variety of environmental contaminants use IRIS as a source for EPA scientific opinion on the potential effects. EPA sees IRIS as a primary mechanism for communicating technical scientific information on potential chronic human health hazards to Agency risk assessors and to trained outside users. The Agency's goal is that IRIS contain high-quality human health information, based on credible science.

Availability of Background Paper

As one step in the ongoing development of this widely used data base, EPA is reevaluating several aspects of IRIS. This evaluation, described below (see Internal Review of IRIS and Request for Comment), is being conducted in a manner that reflects the history, purposes, and goals that led to the initial development of IRIS. This review takes into consideration the current processes used by the two Agency scientific work groups responsible for developing the health hazard information in IRIS.

Therefore, EPA has developed and is making available an IRIS Background Paper that contains the contextual information described above. For those generally unfamiliar with the intent and history of IRIS, this paper will serve as a primer for that information. For those who are regular IRIS users, the paper details the current processes used to develop the health hazard information on IRIS, especially regarding activities of the work groups responsible for developing IRIS information. Interested persons are strongly encouraged to obtain this paper as it provides background information for this **Federal Register** notice and helps to better understand the context of the Agency's internal review of IRIS.

Internal Review of IRIS and Request for Comment

As part of an Agency-wide effort to improve the quality of science used to evaluate and manage risks, and because of growing interest in IRIS and its role as a widely used resource throughout the risk assessment and risk management community, EPA has begun a review of processes by which the information in IRIS is developed and maintained. The purpose of this review is to seek ways to improve how IRIS information is developed and how it is being used by risk managers.

The Agency has convened a team to address issues involving the quality of information and service IRIS provides those who use the system, both inside and outside the Agency. The goal of the team is to study the entire IRIS process, from nomination of substances through delivery of information. The team has been asked to provide a series of recommendations to senior Agency managers to improve quality, including consideration of increased public involvement and additional peer review and more efficient and timely processes. To achieve this goal, the team may address concerns that could include: public involvement, peer review, limitations of IRIS information for risk management decisions, and balancing the addition of new substances with updates of existing information. Issues related to the adequacy of resources devoted to the system, improved efficiency and timeliness of the process for adding and updating files, effective mechanisms for issue resolution, the quality of and need for regulatory action information and supplemental data, outreach and training, and science and methodological issues may also be considered in the future.

As a first step in the team's effort, EPA is focusing on two issues, public involvement and external peer review. For the purposes of this effort, public involvement is defined as opportunities for affected or interested parties to have some level of input into IRIS health hazard information. These groups or individuals can involve a broader spectrum of participants than external peer review. External peer review is defined as critical appraisal of Agency products by independent experts who are peers of those who generate them.

Current practices for public involvement and peer review are described in detail later in this notice and in the IRIS Background Paper, respectively. Briefly, under current peer-review procedures, the technical bases for the oral reference dose, inhalation reference concentration, and cancer information on IRIS undergo various levels of internal peer review by EPA scientists familiar with the substance at issue. In addition, many undergo external peer review from groups ranging from the Agency's Science Advisory Board and the Office of Pesticide Programs's Science Advisory Panel to specially-convened peer-review panels and workshops. EPA is seeking ways to address concerns for increased and improved public involvement and external peer review.

The Agency wishes to identify mechanisms that can involve qualified outside scientists and members of the public in improving the quality of information in IRIS, while not unduly delaying the process of adding critical new information to the data base. Because EPA is bound by statutory and public mandates and schedules, the impact of increased public involvement and peer review on the ability of EPA work groups to develop the IRIS information and on the ability of the data base itself to deliver the information to EPA programs and regions in a timely manner will also be taken into consideration by the team.

In this notice, EPA requests comments from the public on these two issues. The Agency requests information from interested persons on how and how often they use IRIS information and how it affects their decision making. The Agency also requests comments on the following issues relating to peer review and public involvement:

Peer Review—

1. Should decisions made by the EPA work groups responsible for developing the health hazard information on IRIS have further peer-review by scientists outside the Agency?

2. What are the advantages and value (to EPA, the regulated community, and the public) of adopting an enhanced peer-review system for IRIS information? What are the disadvantages and problems?

3. What kind of peer-review system should the Agency consider in view of the significant statutory, public mandates, resource and time constraints related to IRIS and its users? What specific approach or mechanisms should the Agency explore?

Public Involvement—

1. As described later in this notice, EPA provides several current opportunities for public involvement and input into IRIS. What are the advantages and disadvantages of developing further avenues for public participation in the IRIS processes?

2. What are specific other opportunities for improving the science and value of IRIS by involving the public?

3. What should be the goals and objectives of further public involvement given the significant statutory, public mandates, resource and time constraints related to IRIS and its users? What specific approach or mechanisms should the Agency explore?

The Agency would especially welcome suggestions from members of the public experienced in various forms of peer review regarding how we can tailor any peer review to assure optimum use of scientific talent, both within and outside the Agency, and available resources in addressing the most important scientific issues raised. Since the team is in the process of gathering information that relates to public involvement and peer review issues, comments should be focused on those areas. If parties submit comments pertaining to issues other than those of public involvement and peer review, they will be catalogued and reviewed when that issue is taken up by the team. Other issues related to IRIS are expected to be considered at a later time in 1993.

While the Agency will continue to accept informal comments as it evaluates the IRIS processes, the most helpful comments will be those received within 45 days from date of this notice.

Please direct written comments, an original and one unbound copy, to the IRIS Quality Action Team at the address given in the beginning of this notice. Public comments will be considered in developing options for improved processes for IRIS. EPA will summarize and address the comments received in a subsequent **Federal Register** notice.

Materials submitted to the Agency in response to this request for comments on the Internal Review activity can be inspected in the following two ways:

1. In person at the Office of Research and Development (ORD), Public Information Shelf, EPA Headquarters Library, 401 M Street SW., Washington, DC 20460. The EPA Headquarters Library is open from 10 a.m. to 4 p.m., Monday through Friday except for Federal holidays. Requests for copies of these materials cannot be handled by phone. If you have any questions about the procedures for the EPA Library, call 202–260–5922.

2. By sending a written Freedom of Information request for the materials you need to: Jeralene Green, Freedom of Information Officer, A–101, USEPA, 401 M Street, SW., Washington, DC 20460.

Under EPA's Freedom of Information Act procedures, there is no charge for duplication of the first 166 pages requested. For detailed information on costs, call the Freedom of Information Office at 202–260–4048.

Current Opportunities for Public Involvement in the IRIS Process

As detailed in the companion piece to this notice, the IRIS Background Paper, there are several points in the current IRIS process where public input is encouraged. IRIS users are invited to participate in the IRIS information development process. Four current methods for public involvement and input are listed below in a suggested hierarchical order of use. They are:

1. IRIS Scientific Contacts

Since 1988, when IRIS was made available to the public, the names and telephone numbers of two EPA staff who are the scientific contacts for a specific assessment have been included on the data base. The Agency believes that the inclusion of Agency scientific contacts able to discuss the basis for the Agency's position is very important. These individuals play a major role in providing public access to IRIS and provide a conduit for valued public comment.

2. IRIS Public Reading Room

Another opportunity for information access is a newly created IRIS Public Reading Room located in the library facility in the Andrew W. Breidenbach Research Center, U.S. EPA, 26 West Martin Luther King Drive, Cincinnati, OH, which is scheduled to open in the Spring of 1993.

The IRIS Public Reading Room has information related to substances on IRIS. It does not have copies of correspondence submitted in response to the Agency's request for comments on the internal review of IRIS that was outlined above. To review those comments, follow the directions detailed in the **Internal Review of IRIS and Request for Comment** section of this notice.

Visitors will be able to review the documentation files for substances on IRIS. These files contain the background and supporting material, including a synopsis of the scientific discussion underlying the RfDs, RfCs, and carcinogenicity information that are on IRIS. The files also may include the following: CRAVE and RfD/RfC Work

Group meeting notes, IRIS printouts with bibliographies, public information submissions, correspondence, and annotated literature searches. Files for substance assessments not yet on the system will not be available for viewing.

Individuals wishing to review the documentation files for substances on IRIS should contact the Cincinnati office to schedule an appointment. The IRIS files can be viewed by appointment only. Appointments should be scheduled at least one week in advance and interested persons should identify the specific substances they wish to review at that time. For more information on the IRIS Public Reading Room or to make an appointment, contact IRIS User Support (operated by Computer Sciences Corporation) at (513) 569–7254.

The IRIS Public Reading Room is only a first step in providing increased access to IRIS processes. At this time, the Agency is unable to respond to informal requests for paper copies of the files. As part of the internal review of IRIS described previously, the Agency is evaluating other means of increased public access.

3. IRIS Information Submission Desk

The most important of the current opportunities is the IRIS Information Submission Desk that was set up in 1988 when the data base became publicly available. The Desk staff distribute submissions to the appropriate Agency offices for subsequent use in the IRIS information development processes.

The most useful submissions are those received on substances that are scheduled for initial work group review in the near future. This permits timely and thorough review and consideration of a submission as an integral part of the work groups' scientific deliberations. EPA hopes that the list of substances scheduled for work group review contained in this notice will prompt submission of scientific comments and analysis, studies, and identification of other pertinent scientific information from interested persons. New studies and other information on substances already on IRIS are also welcomed.

Submissions to the IRIS Information Submission Desk are handled in a three-step process:

First, interested persons should simply provide a list (submission inventory) and briefly identify all the information that they wish to submit to the IRIS Information Submission Desk. This submission inventory could include studies, statistical analyses, or comments on data interpretations. If appropriate, the materials should be listed using scientific citation format, that is, author(s), title, journal, and date. The submitter will receive an acknowledgement of receipt of the submission inventory.

It is important to note that interested persons should only include information that they believe the Agency would not otherwise have, such as unpublished studies or other studies not available through standard literature searches. Published scientific literature that is readily identifiable and obtainable should not be submitted to the Desk; this information is gathered during the standard work group review process. The use of the preliminary submission inventory will help prevent an influx of duplicative information.

The submission should include:

A. A cover letter that:

- States that the correspondence is an IRIS information submission;
- Describes in general terms the purpose of the submission; and
- Includes the names, addresses, and telephone numbers of persons to contact for additional information on the submission.

B. A submission inventory of all materials that persons wish to submit that:

- Identifies the substance(s) by name and Chemical Abstracts Service (CAS) number(s). If the submission is not related to a specific substance, but related to an issue(s) such as dose-response extrapolation methods, this should be clearly stated;
- States the section of IRIS (for example, oral reference dose, inhalation reference concentration, inhalation carcinogenicity assessment, etc.) that is being addressed; and
- Lists and describes briefly the information or supporting documents suggested for consideration.

In the second step, EPA will identify from the submission inventory the information that should be submitted. The submitter will receive notification requesting submission of the selected material. If certain pieces of information are not requested for submission, an explanation will be provided to the sender.

In the third step, the submitter should send in copies of the information requested by the Agency using the following format:

- Submitters should send three copies (at least one of which should be unbound);
- Submitters should identify the substance(s) by name and Chemical Abstracts Service (CAS) number(s);
- Persons submitting health effects data for substance files already on IRIS should include, for each study submitted, a specific explanation of how and why the study results could change a quantitative risk value or relevant IRIS narrative; and
- Persons submitting health effects data for those substances scheduled for consideration by the work groups should include, for each study submitted, an explanation of the significance of the study results to a potential RfD or RfC, carcinogen assessment value, etc.

Submitters are cautioned that:

- Health effects data on substances subject to the reporting rules under Section 8(d) of the Toxic Substances Control Act (TSCA) must be submitted to the address given in the rule. Submitting them to the IRIS Information Submission Desk does not relieve persons from an 8(d) reporting requirement,
- All submissions are public information,
- Confidential Business Information (CBI) should not be submitted to the IRIS Information Submission Desk. CBI must be submitted to the appropriate office via approved Agency procedures for submission of CBI as codified in the Code of Federal Regulations (40 CFR, Part 2, Subpart B),
- If a submitter believes that a CBI submission contains information with implications for IRIS, it should be noted in the cover letter accompanying the submission, and
- Any materials marked Confidential will be immediately returned to the submitter.

Once a submission has been evaluated and appropriate work group review and conclusions recorded, a letter will be sent to the submitter, briefly describing how the information was evaluated and used.

Comments on Drinking Water Health Advisories or regulatory summary information will not be considered by the IRIS Information Submission Desk unless the commenter identifies an inconsistency between the information summarized in IRIS and the actual USEPA Office of Drinking Water Health Advisory or EPA regulatory information. Questions about Drinking Water Health Advisories should be addressed to the Safe Drinking Water Hotline (1–800–426–4791) or the other EPA contact listed for that section on IRIS. Although EPA regulations are summarized in IRIS, letters on the content of regulations will not be considered by the IRIS Information Submission Desk; they should be addressed to the EPA program office responsible for the regulatory action.

Information submissions should be sent to: IRIS Information Submission

Desk, USEPA, Environmental Criteria and Assessment Office (MS–190), 26 Martin Luther King Drive, Cincinnati, OH 45268.

4. Scientific Seminars

A fourth avenue for public input into development of EPA risk information is to organize a scientific seminar with scientists from EPA. Requests for a seminar can be originated either by interested outside scientists or by EPA scientists.

This is an opportunity for exchange of ideas on either a general scientific issue or on a substance-specific topic. However, these scientific seminars may not include policy issues. Scientific seminars have been used in the past to examine new approaches to health assessment and differences in data interpretation of key studies. These scientific discussions are invaluable during review of a substance.

Scientific seminars should be coordinated with interested staff in all appropriate program and research offices.

Public Access to IRIS

There are currently two means of public access to the IRIS data base. These are supported as official versions of IRIS by the Agency. For further information on these access methods, please call IRIS User Support at (513) 569–7254.

1. TOXNET

The primary method of access for the private sector is the TOXicology Data NETwork (TOXNET), which is maintained by the National Library of Medicine (NLM), National Institutes of Health. IRIS has been a component of TOXNET since 1990.

TOXNET is an on-line integrated system that is flexible in search, print, and other commands. Users can easily and quickly extract data either on entire or selected portions of a specified data field. TOXNET provides sophisticated search and retrieval features for NLM users.

IRIS on TOXNET is updated at the beginning of each month with new information, modifications, deletions, revisions, and notification of pending actions, as needed. IRIS users can gain access to TOXNET by direct call or through several widely used telecommunications networks. IRIS on TOXNET is also available through NLM's International MEDLARS Centers. For further information on gaining access to IRIS via TOXNET, contact: IRIS Representative, Specialized Information Services Division, National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894, Telephone: (301) 496–6531.

2. National Technical Information Service

IRIS is also available on high density 5¼" floppy diskettes that may be purchased from the National Technical Information Service (NTIS). The files are in ASCII format and are intended for use with a text editor. IRIS diskettes are updated quarterly, while the IRIS data base is updated monthly; therefore, NTIS diskettes will not always reflect the most current IRIS information. For information on ordering IRIS diskettes, contact: National Technical Information Service, US Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161, Telephone: (703) 487–4650.

The order number for a single set of diskettes is PB91–591331: for a quarterly subscription, the number is PB91–591330. Call (800) 553–6847 for RUSH orders.

Work Group Substance Review Schedule and Data Solicitation

The following substances are tentatively scheduled for review by EPA work groups during the period from March 1, 1993 to December 31, 1993. The list of substances includes those that will be evaluated by the work groups for the first time and those that are being revisited. In the list below new substances are designated by N and revisits by R.

To submit information to the IRIS Information Submission Desk, follow the guidelines outlined previously. Also, this list of substances, with appropriate updates if necessary, is also expected to be available on IRIS itself in the near future. If you have questions, please call IRIS User Support at (513) 569–7254.

Name	CAS. No.	N/R
Carcinogen Risk Assessment Verification Endeavor (CRAVE)		
Acetylaminofluorine, 2-	53–96–3	N
Acifluorfen	62476–59–9	R
Beryllium	7440–41–7	R
Boron	7440–42–8	R
Bromoacetic acid	79–08–3	N
Bromacil	314–40–9	N
Carbofuran phenol	1563–38–8	N
Chloroacetic acid	79–11–8	N
Chloral hydrate	302–17–0	N
Chlorine dioxide	10049–04–4	N
Chlorite	14998–27–7	N
Chlorate	14866–68–3	N
Chloromethane	74–87–3	R
Cyanazine	21725–46–2	R
Dibromoacetic acid	631–64–1	N
Dibromo-3-chloropropane, 1,2-	96–12–8	R
Dicamba	1918–00–9	R
Dichloroacetic acid	79–43–6	N
Dichloropropane, 1,2-	78–87–5	N
Dichloropropene, 1,3-	542–75–6	R
Dimethyl aminoazobenzene	60–11–7	N
Dimethylcarbamoyl chloride	79–44–7	N
Dimethylhydrazine, 1,1-	57–14–7	N
Dinitrotoluene, 2,4-	121–14–2	R
Environmental tobacco smoke	—	N
Ethyl carbamate	51–79–6	N
Ethyleneimine	151–56–4	N
Ethylene oxide	75–21–8	N
Formaldehyde	50–00–0	R

Name	CAS. No.	N/R
Ethylene thiourea (ETU)	96-45-7	R
Methomyl	16752-77-5	R
Methylaziridine, 2-	75-55-8	N
Methylbenzenamine, 2-	95-53-4	N
Methylenebis (2-chloroaniline), 4,4'-	101-14-4	N
Methyl iodide	77-88-4	N
Methyl tert-butyl ether	1634-04-4	N
Metolachlor	51218-45-2	R
Molybdenum	7439-98-7	N
Nitropropane, 2-	79-46-9	N
N-Nitroso-N-methylurea	684-93-5	R
Pentachloronitrobenzene	82-68-8	N
o-Phenylenediamine	95-54-5	N
Prometon	1610-18-0	N
Propane sultone, 1,3-	1120-71-4	N
Quinoline	91-22-5	N
Tetrachloroethylene	127-18-4	R
Toluene-2,4-diamine	95-80-7	N
Trichloroacetic acid	76-03-9	N
Trichloroethylene	79-01-6	R
Trichloropropane, 1,2,3-	96-18-4	R
Vinyl chloride	75-01-4	R

Oral Reference Dose/Inhalation Reference Concentration Work Group (RfD/RfC Work Group)

RfD Verification

Acetone	67-64-1	R
Aroclor 1248	12672-29-6	R
Aroclor 1254	11096-82-5	N
Beryllium	7440-41-7	R
Boron	7440-42-8	R
Bromomethane	74-83-9	R
Cadmium	7440-43-9	R
Chromium (III)	16065-83-1	R
Chromium (VI)	18540-29-9	R
Cobalt	7440-48-4	R
Dichloropropene, 1,3-	542-75-6	R
Di-N-octyl phthalate	117-84-0	N
Hydrazine	301-01-2	N
Mercury (inorganic)	7439-97-6	R
Methyl ethyl ketone peroxide	1338-23-4	R
Methyl isobutyl ketone	108-10-1	R
Methyl mercury	22967-92-6	R
Methylphenol, 2-	95-48-7	R
Methylphenol, 3-	108-39-4	R
Methylphenol, 4-	106-44-4	R
Naphthalene	91-20-3	R
N-Nitrosodiphenylamine	86-30-6	N
Terphenyl	26140-60-3	N
Thiophenol	108-98-5	R
Trichloroethane, 1,1,1-	71-55-6	R

RfC Verification

Acetonitrile	75-05-8	R
2-Acetylaminofluorene	53-96-3	N
4-Aminobiphenyl	92-67-1	N
Anthracene	120-12-7	N
Arsenic, inorganic	7440-38-2	N
Benzene	71-43-2	R
Benz(a)anthracene	56-55-3	N
Beryllium and compounds	—	R
Butadiene, 1,3-	106-99-0	N
Cadmium and compounds	—	R
Calcium cyanamide	156-62-7	N
Carbon disulfide	75-15-0	R
Carbon tetrachloride	56-23-5	N
Chlordane	57-74-9	R
Chlorine	7782-50-5	R
Chloromethane	74-87-3	R
Chromium and compounds	—	R
Cobalt and compounds	—	N
Coke oven emissions	8007-45-2	N
Cumene	98-82-8	R
Dibromodifluoromethane	75-61-6	N
Dichloro-2,2,2- trifluoroethane, 1,1-	306-83-2	R
Dichloromethane	75-09-2	R
Dichloroethane, 1,1-	75-34-3	R
Dichloroethylene, 1,1-	75-35-4	R
Difluoromethane	75-10-5	N
Dioxane, 1,4-	123-91-1	N

Name	CAS. No.	N/R
Ethylene oxide	75–21–8	N
Ethyl acrylate	140–88–5	N
Fluoranthene	206–44–0	N
Hepatfluoropropane,1,1,1,2,3,3,3-	431–89–0	N
Hydrogen fluoride	7664–39–3	R
d-limonene	5989–27–5	N
Manganese	7439–96–5	R
Mercury and compounds	—	R
Methyl isobutyl ketone	108–10–1	R
Methyl methacrylate	80–62–6	N
Methyl tert-butyl ether	1634–04–4	R
Methylene dianiline, 4,4-	101–77–9	R
Naphthalene	91–20–3	N
Nickel and compounds	—	R
Nitrobenzene	98–95–3	R
N-Nitrosomorpholine	59–89–2	N
N-Nitroso-N-methylurea	684–93–5	N
Pentachlorobenzene	608–68–8	N
Pentafluoroethane, 1,1,2,2,2-	354–33–6	N
Decafluorobutane	355–35–9	N
Tetradecafluorohexane	355–42–0	N
Phenanthrene	85–01–8	N
Phosphorous	7723–14–0	N
α-Pinene	80–56–8	N
β-Pinene	127–91–3	N
Polychlorinated biphenyls	1336–36–3	N
Polycyclic organic matter	—	N
Pyrene	129–00–0	N
Selenium	7782–49–2	N
Silica compounds	—	N
Styrene oxide	96–09–3	N
Tetrachloroethane, 1,1,2,2-	79–34–5	N
Tetrachloroethylene	127–18–4	N
Tetrafluoroethane, 1,1,1,2-	811–97–2	R
Tetrahydrofuran	109–99–9	R
Trichloroethane, 1,1,1-	71–55–6	R
Trichloroethylene	79–01–6	R
Trifluoroethane	420–46–2	N
Trifluoromethane	75–46–7	N
Vinyl chloride	75–01–4	N

A list of the substances scheduled for work group review from January 1, 1994, to June 30, 1994, will be published in the **Federal Register** in June/July, 1993.

Dated: February 12, 1993.

Gary J. Foley,

Acting Assistant Administrator for Research and Development.

[FR Doc. 93–4397 Filed 2–24–93; 8:45 am]

BILLING CODE 6560–50–P

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

March 1, 1993

OFFICE OF
RESEARCH AND DEVELOPMENT

Dear IRIS User:

The recent FEDERAL REGISTER notice and background paper on the EPA's Integrated Risk Information System (IRIS) are enclosed for your review and comment. These two documents have been sent to you because you are either a current IRIS user or have expressed an interest in Agency activities regarding IRIS.

The FEDERAL REGISTER notice has three main purposes. First, it announces the availability of the enclosed background paper describing IRIS, its contents, and the current processes used by the two Agency work groups responsible for developing the IRIS information. Second, it discusses an Agency activity to review IRIS processes, solicits comments on this process, and highlights points in the current process where public input is encouraged. Third, it announces a new process for publication of a list of the substances scheduled for IRIS work group review and the solicitation of pertinent data, studies, and comments on these substances.

Although the Agency is keenly interested in how you view IRIS and its use as a risk assessment tool and continues to encourage the submission of comments in that regard at any time, I urge you to review the enclosed documents and provide your comments on the internal review of IRIS as outlined in the notice within the 45 day comment period. Also, if you are aware of any pertinent data, studies, or other unpublished scientific literature on any of the substances listed in the notice as scheduled for future work group review, I invite you to submit them to the Agency per the detailed instructions included in the notice.

Thank you for your attention to this matter.

Sincerely yours,

William H. Farland, Ph.D.
Director
Office of Health and Environmental Assessment

Enclosures