

Toxicology Excellence for Risk Assessment



TERA

a nonprofit corporation dedicated to the
best use of toxicity data for risk values

June 10, 2009

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Representative Paul Broun, M.D.
Subcommittee on Investigations and Oversight
Committee on Science and Technology
U.S. House of Representatives
394 Ford House Office Building
Washington, DC 20515

Dear: Dr. Broun

I strongly encourage, without reservation, broad scientific collaboration in order for EPA's IRIS process to meet the needs of the 21st century. Specifically, based on my experience,¹ training, and discussions with EPA staff, as well as scientists from many interested groups, I highly recommend that EPA:

- Clarify the process of involvement with the scientific community; the process for resolving scientific disagreements among interested parties needs to be explicit.
- Work with outside groups with appropriate conflict restrictions to bring in data, opinions, and solutions to complex problems. EPA does not have all the answers. Balancing our individual and group biases will yield better science.
- Allow sufficient time and opportunities for discussion of scientific issues, for example, a 60-day comment period (as in rulemaking) for all parties; EPA should recognize that resolution of scientific issues will take longer.
- Enhance training of EPA staff in dose response assessment techniques, and mentors its younger staff to the artisan and expert levels; many EPA staff do not know basic dose response assessment information.
- Develop safe dose values by scientific consensus among EPA offices and fellow federal agencies, and outside experts as appropriate.

¹ Prior to working at Toxicology Excellence for Risk Assessment (TERA) for 15 years, I worked for 15 years at the U.S. Environmental Protection Agency (EPA), holding several leadership roles on specific key projects, including the creation of EPA's IRIS.

A Brief History of IRIS

IRIS is a national treasure, held in trust by the EPA for all of us.²

It has not always been this way, however.

IRIS first started in 1986, as a mechanism to harmonize "safe" dose values³ among EPA program offices, after it was found that 39 of 40 values for chemicals derived by separate program offices were different from each other. Only one chemical had similar values developed by different program offices; however, this single instance of congruence happened by luck, not by scientific reasoning. This dismal record of 0 for 40 was due in part to the enormous workload of staff and the general lack of communication among EPA offices doing safe dose assessment work.

Within 5 years, EPA had created IRIS to house unanimous consensus information for 500 chemicals. This remarkable turnaround came about through collaborative work among senior EPA scientific staff on two agency peer review work groups,⁴ and the commitment of EPA management. Different EPA offices proposed risk values, which were reviewed in monthly internal meetings; values with which everyone agreed were loaded on IRIS. Senior scientific staff among EPA offices interacted on numerous safe dose deliberations prior to work group review and younger staffers had training in preparation for agency work group meetings.

During the early 1990s the influence of IRIS grew and the risk values were being used in many regulatory and enforcement situations; states, industries, and other interested parties petitioned EPA to reconsider many values based on newer data and analysis. Unfortunately, EPA had few dedicated resources for such reconsiderations,⁵ and as a result, EPA's polite letters of reply were often followed by years of EPA inactivity.

Due to this intense scrutiny and the receipt of resources in the latter 1990s, EPA management began a process of IRIS consolidation. One of the casualties of this consolidation was the abandonment of the successful work groups, and the dwindling of collaborative spirit among agency offices soon followed. Several reorganizations of the IRIS process have been proposed since the late 1990s, the latest is under discussion today.

² Dourson M. and J. Patterson. 2004. The Integrated Risk Information System: Challenges and Opportunities. Risk Policy Report. 11(5): 29-31.

³ "Safe" doses within EPA go by the name of Reference Dose or (RfD) for noncancer toxicity oral exposures, Reference Concentration (RfC) for noncancer toxicity inhalation exposures, or Oral Slope Factors (OSF) for cancer toxicity oral exposures or Inhalation Unit Risk for cancer inhalation exposures.

⁴ The RfD/RfC work group for noncancer toxicity, and the Carcinogen Risk Assessment Verification Endeavor (CRAVE) work group for cancer toxicity.

⁵ In the early 1990s, 75 requests for reconsideration were pending. Each request was estimated to require the use an average of \$10,000 in extramural funds and 0.1 FTE, or total funds of \$750,000 and 7.5 FTE. In contrast, EPA had a total of 0.3 FTE in dedicated resources and no extramural funds (M. Dourson, personal recollections).

But IRIS as a repository representing the best Agency safe doses has been lost.

Fully one quarter of all IRIS values do not reflect the latest EPA safe doses.⁶ In particular, the Office of Pesticide Programs (OPP) of EPA has developed or revised risk values based on the most recent available data for numerous substances, yet these newer values are not available on IRIS. Developing a process that provides for timely development of risk values, while allowing for full engagement by representatives from the relevant program offices, will allow IRIS to resume its former place as the comprehensive site for EPA risk values.

2009 IRIS Process

The 2009 IRIS process has the advantages of a tightened time frame and clearer entry points for deliberations, and will serve well for many of the chemicals assessed within the program that have limited scientific issues and environmental impact (e.g., a chemical is found at only a few Superfund sites). However, the proposed 2009 process will not work for chemicals with major scientific issues and environmental impact (e.g., dioxin) without a significant increase in the timeline, as EPA acknowledges. In such cases, EPA's process must:

- Allow time in the schedule when key studies are ongoing, planned, or, under development; for example, we now have much better knowledge of perchlorate's toxicity due to over 5 million dollars of research since 1997; this knowledge has led to a more credible safe dose.
- Ensure that the public listening session is directly tied to the external peer review, and that peer reviewers are present or aware of the points raised.
- Define criteria for use of EPA's Science Advisory Board or the NAS reviews; also, these panels need to include a sufficient number of erudite risk assessment scientists, and preferably be chaired by one of them.

More importantly, EPA's IRIS staff needs to listen.

The single, most intense frustration on the IRIS process, made by many erudite scientists, both inside and outside EPA, is that EPA's IRIS staff will not listen to, or is not capable of understanding, their scientific comments. Several of these folks have told me that they see no point in further research on mode of action (MOA) because it will not be fully, or even partially, considered by EPA IRIS staff. This is particularly worrisome, since EPA's well-written cancer risk assessment guidelines⁷ emphasizes MOA understanding in cancer assessments.

The process for resolving scientific disagreements within the agency and between EPA and other agencies is not clear in the current reorganized process. Are key decisions made by consensus, or will one scientist have the final say? Most scientists have a bias one way or

⁶ See EPA IRIS list of substances and focus on files with OPP Reregistration documentation at www.epa.gov/iris.

⁷ U.S. Environmental Protection Agency. 2005. Guidelines for carcinogen risk assessment. Washington D.C. EPA/630/P-03/001B.

another (for example, as a toxicologist, I am biased when reviewing epidemiology studies in one direction). Thus, if a decision is made only by one scientist then it will likely be biased in one direction. It is only in the collective balancing of biases that the best science can be brought forward, much like the intersection of multiple events in a Venn diagram.

In contrast, the resolution of disagreements in the EPA 2008 IRIS reorganization seemed more clear with a very deliberative process for chemicals of high impact to environmental protection. For example, the safe dose for perchlorate was eventually determined by a panel of scientists from the National Academy of Sciences to be 25 times higher than what EPA proposed. But this panel only came about after a more deliberative process involving several federal agencies, and several years of intense work, including numerous research studies, similar to what the 2008 IRIS reorganization suggested.

Do reorganizations matter?

Perhaps more important than any reorganization, however, is the incorporation of flexibility in the overall process based on the determination of working relationships among all participants. In the early days of IRIS, the EPA program and research offices communicated poorly. Forcing discussions among EPA offices soon fostered a scientific, collaborative spirit, which not only built IRIS to 500 chemicals in 5 years but also trained younger staff to be better risk assessment scientists. A key aspect of this process was that the scientists from different offices discussed the assessments and reached resolution on key recurring issues. This collaboration also assisted the development of EPA-wide risk assessment guidelines and research to improve the basis of risk assessments.

While the 2009 process, suitably amended, will provide opportunities for EPA and other scientific agencies and outside parties to discuss scientific issues, it does not appear to provide similar opportunities for discussion within the EPA among different offices. Direct communication and collaboration amongst EPA staff is also essential to insure that the best science is incorporated into the IRIS assessments. The fact that the current IRIS process is not looked upon favorably by many EPA staff attests to this failure within EPA to communicate.

Scientific collaboration with all interested parties, could propel EPA's IRIS process, and the science and practice of risk assessment, forward to meet the needs of the 21st century. I strongly encourage, without reservation, such a collaborative spirit; for it is only in our collective efforts that we will best protect the public's health.

Nothing less should be expected of us.

Sincerely,

A handwritten signature in black ink that reads "Michael L. Dourson". The signature is written in a cursive style with a large, sweeping initial "M".

Michael L. Dourson, Ph.D., DABT, ATS

President

Toxicology Excellence for Risk Assessment (*TERA*)⁸

⁸ Toxicology Excellence for Risk Assessment (*TERA*) is a non-profit, 501(c)(3) corporation that develops partnerships among government, industry and other interested groups to address risk assessments of high visibility (such as formaldehyde, perchlorate, and soluble nickel) and cooperative ventures such as the Voluntary Children's Chemical Exposure Program (VCCEP), the International Toxicity Estimates for Risk (*ITER*) database, the Risk Information Exchange (RiskIE) database, and the Alliance for Risk Assessment (*ARA*). *TERA*'s funding sources are primarily government agencies (such as EPA, NIOSH, FDA, Health Canada, and U.S. States--at 67% in 2008). *TERA* also accepts funding from DoD and industry, if the sponsors accept its conditions of publication.

See also <http://toxnet.nlm.nih.gov/> for *ITER*, and <http://www.allianceforrisk.org/> for RiskIE and the *ARA*.



***TERA* Statement of Purpose**

Toxicology Excellence for Risk Assessment (***TERA***) is a non-profit, 501(c)(3) corporation organized for scientific and educational purposes. Our mission is to protect public health by developing and communicating risk assessment information, improving risk methods through research, and educating the public on risk assessment issues. Some specific activities of ***TERA*** are listed below.

- Establish high-quality risk assessment values based on the latest scientific data and methods through the **Verifiable Estimates for Risk Assessment (*VERA*)** program
- Provide a unique side-by-side comparison of hazard values, information and dose response from organizations and independent parties worldwide through the **International Toxicity Estimates for Risk (*ITER*)** Database
- Conduct research to improve the underlying methods for human and ecological risk assessment
- **Peer Review and Consultation** of risk information, methods and study designs through an independent and public process
- **Educate** diverse groups on risk assessment issues, through training courses, scientific support and the State Hazard Evaluation Lending Program (**State HELP**)
- Improve the practice of **risk assessment** through independent and objective guidance and advice

TERA is a non-profit corporation organized under section 1702.01 of the Ohio Revised Code, and is classified as a 501(c)(3) organization under the Internal Revenue Service Code. Corporations, companies, associations, individuals and foundations may support the work of ***TERA*** through tax-deductible contributions.