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Fostering Quality Science at EPA: Perspectives on Common Sense Reform

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Summary

The American Chemistry Council[1] (ACC) very much appreciates this opportunity to provide testimony on common sense measures to foster quality science at the Environmental Protection Agency (EPA) and throughout the federal government.

The business of chemistry is fundamentally the business of science. This business of science is a critical component for manufacturing safe products required to house, feed, and protect people in the United States as well as provide for the tremendous quality of life experienced by American citizens who enjoy many high quality and safe consumer goods that were unavailable just a few decades earlier. ACC member companies rely on science to conduct the research necessary to discover new chemistries and identify new applications of existing chemistries. They also rely on science to develop new tools for assessing the potential hazards, exposures and risks of chemical substances. As one of the Nation's most regulated industries, ACC member companies similarly expect high quality science – and reliable assessment processes – to underpin effective and efficient regulatory decisions by the Federal government.

Unfortunately, processes for conducting and reviewing chemical assessments at EPA and other government agencies are not always based on the consistent use of the best available science. The lack of scientific quality and reliability directly compromises societal access to cost effective and safe products that house, feed, and protect us while making life more enjoyable at the same time. While there has been much recent focus on EPA's Integrated Risk Information System (IRIS), the problems identified by the National Academy of Sciences (NAS) in the IRIS program are also evident in other government chemical assessment programs.

EPA has acknowledged many of the deficiencies in the IRIS program, and is taking some welcome steps to address the concerns identified by the NAS. EPA is also making an important effort to develop and evaluate emerging technologies to improve chemical assessments, and ACC has been pleased to support these efforts.

ACC's testimony today outlines a number of recommendations to improve the quality and process of science at EPA and more broadly through the Federal government. The following areas should receive particular attention:

- Improving the quality of science through sound risk assessment processes, standards and criteria.
- Improving the quality of science through enhanced peer review.
- Enhancing the quality of science by leveraging emerging science and technology.

[1] The American Chemistry Council (ACC) represents the leading companies engaged in the business of chemistry. ACC members apply the science of chemistry to make innovative products and services that make people's lives better, healthier and safer. ACC is committed to improved environmental, health and safety performance through Responsible Care®, common sense advocacy designed to address major public policy issues, and health and environmental research and product testing. The business of chemistry is a $674 billion enterprise and a key element of the nation's economy. It is one of the nation's largest exporters, accounting for ten cents out of every dollar in U.S. exports. Chemistry companies are among the largest investors in research and development. It is also one of the nation's most heavily regulated industries.

I. Improving the Quality of Science through Sound Risk Assessment Processes, Standards and Criteria

The Subcommittee's inquiry into the level, quality, usefulness and objectivity of science at the Environmental Protection Agency (EPA) is timely. There are well-known deficiencies in EPA's Integrated Risk Information System (IRIS) – deficiencies that Congress has directed the National Academy of Sciences to review. But the problems that affect the Agency's ability to assure that the science generated, reviewed and used is of the highest quality are not unique to EPA.[2] ACC's testimony today outlines a number of recommendations to improve the quality and process of science at EPA and more broadly through the Federal government.

At the heart of the problem in the Federal government's processes for assessing risks to environment and human health is the lack of a consistent, coherent, science-based framework that binds the agencies to an appropriate and transparent approach for weighing evidence, considering uncertainty, and keeping up with advances in the field. The processes for considering scientific information and data and the standards and criteria used in risk assessment need to be modernized and streamlined to meet both today's needs and greater challenges of the future.

A. Integrated Risk Information System (IRIS)

Despite continued evolution of the EPA IRIS process, specific fundamental improvements to the program are necessary to ensure that IRIS assessments developed by EPA are firmly based on up-to-date scientific knowledge, meet the highest standards of scientific inquiry and integrity, and are evaluated in accordance with acceptable scientific approaches.

IRIS is used by EPA as the primary source of information regarding the potential adverse human health effects of chemicals. IRIS is also a leading source of health risk information for other federal, state, and international regulatory bodies. Given the importance that IRIS evaluations have for EPA program offices, other federal agencies, and state governments, as well as their impacts on the private and public sectors, it is clear that significant improvements are warranted and long overdue.

[2] EPA's Integrated Risk Information System (IRIS) has been the focus of much critical attention recently. As the Subcommittee is well aware, the National Academy of Sciences (NAS) has expressed concern over "[t]he persistence of limitations of the IRIS assessment methods and reports . . . particularly in light of the continued evolution of risk-assessment methods and the growing societal and legislative pressure to evaluate many more chemicals in an expedient manner." The NAS report further cites a lack of clarity and transparency as a "repeating theme" over the last decade, insufficient documentation on methods and criteria for identifying evidence from relevant studies, and a lack of information useful in assessing the weight of the evidence, among other problems. These concerns not limited to IRIS, or even EPA. For example, the Report on Carcinogens (RoC) issued by National Toxicology Program (NTP), housed in the Department of Health and Human Services (HHS). The 12th RoC, released in July 2011, makes many of the same methodological errors in its evaluation of formaldehyde as IRIS did in its review, and the 12th RoC's review of styrene conflicts with a 2010 evaluation by another HHS entity. Similar concerns exist with EPA's Clean Air Scientific Advisory Committee.

Many of these necessary improvements were outlined in Chapter 7 of the April 2011, NAS scientific peer review report on formaldehyde and underscored during two recent Congressional oversight hearings on IRIS. Despite general agreement with the need to make the changes recommended by the NAS, EPA has yet to provide further details on how it will implement the NAS IRIS improvements. The U.S. Government Accountability Office (GAO) has called on EPA to develop a clear plan for fixing IRIS.[3]

In an effort to move EPA in this direction, Congress recently passed bipartisan legislation which directs EPA in FY 2012 to:

- Incorporate, as appropriate, the recommendations of Chapter 7 of the National Research Council's Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde into the IRIS Process; and
- Issue a progress report to House and Senate Committees on Appropriations and relevant Congressional authorizing committees no later than March 1, 2012, describing its implementation of the National Research Council's Chapter 7 recommendations for ongoing and new assessments.

This action by Congress rightfully underscores the widespread agreement that more work is needed to improve IRIS so the program delivers scientifically defensible assessments.

EPA does not need to go back to square one to improve IRIS and the assessments already underway. But more than a cursory review and more than simple improvements are needed. In particular, EPA should determine whether all ongoing assessments – including those that the Agency is revising to take into account peer review and public comments – meet the NAS standards for reviewing studies, evaluating weight of evidence, determining mode of action, establishing cause and effect, and for selecting the dose-response method for quantifying potential health risks. If an IRIS assessment falls short, it must be upgraded.

ACC firmly believes that this process can be accomplished without undue delay in making IRIS assessments final. All stakeholders have an interest in IRIS assessments that rely on the best available scientific information regarding hazard and exposure; employ consistent, objective methods and models; utilize transparent evaluation procedures for data quality, cause and effect; and that weigh the full body of scientific evidence. If an ongoing IRIS assessment does not meet these criteria (for example, if a draft IRIS assessment does not employ a robust weight of the evidence approach), the program must accept that more time will be needed to get the assessment right. The credibility of the IRIS program is not enhanced by assessments that fail to address the basic criteria for quality and reliability.

Importantly, there is nothing in the current IRIS program that provides an incentive for companies to develop new data and information, and to use new toxicological methods and tools to generate and gather that data. Indeed, the industry has little confidence that new information

[3] Government Accountability Office, "Chemical Assessments: Challenges Remain With EPA's Integrated Risk Information System Program", GAO-12-42, Dec 9, 2011. Available at http://www.gao.gov/assets/590/586620.pdf.

and data can overcome the conservative default assumptions employed in the program or the persistent problems identified in peer review.

In ACC's view, two principal solutions can help meet the Federal government's need to enhance chemical risk assessment, and to restore credibility in the results. First, federal agency standards for risk assessment need to be updated. Ideally, the same set of updated standards would apply across the Federal government. There are a variety of ways this might be accomplished. Second, the laws and rules governing scientific peer reviews should be updated to make that vital process more effective and transparent.

B. Improved Standards for Risk Assessment

Under existing authority there is a clear role for the Office of Management and Budget (OMB) in reviewing agency assessments, and coordinating a robust interagency review, to promote uniformity in process and results. It is clear that federal risk assessment activities are not being coordinated, despite direction and guidance provided by OMB bulletins and memoranda.[4] Moreover, there is no current government-wide oversight to ensure coordination. As a consequence, the lack of a coordinated approach to these various assessment programs creates the potential for duplication and inconsistent findings. Most troubling, each federal agency conducting such assessments does so in a different way, using different processes and standards.

To address this lack of coordination and consistency, federal agencies need to adopt updated state-of-the-art standards for human health and environmental risk assessments. Ideally, agencies would all follow a consistent set of standards. Agencies should be required to explain how they followed these standards, including providing a clear articulation of reasons for choices they made in the process. Agency compliance with those requirements would be enhanced if it were subject to regular oversight, including judicial review.

Federal standards for risk assessment should:

- Include criteria for evaluating the validity of test methods and the reliability and credibility of data.
- Require an assessment of the weight of evidence regarding hazard and exposure, based on criteria that should include elements such as a systematic review of all relevant and reliable toxicological, epidemiological and mechanistic data, including negative results; a preference for human data, where it is relevant and adequate; and consideration of biologically-plausible modes of action most relevant to humans.
- Require agencies to present the distribution of estimated hazards or risks, including central tendency values.
- Require agencies to characterize uncertainty and variability quantitatively, where feasible, and to explain these and other limitations of the analysis with sufficient clarity to be understood by non-scientists.

[4] OMB "Final Information Quality Bulletin for Peer Review" and OMB's "Updated Principles for Risk Analysis" (http://www.whitehouse.gov/sites/default/files/omb/memoranda/fy2005/m05-03.pdf; http://www.whitehouse.gov/sites/default/files/omb/assets/regulatory_matters_pdf/m07-24.pdf).

- Require full disclosure of:
    - Data, methods and models sufficient to allow independent reanalysis by qualified experts;
    - Rationales for choosing key studies, methods and models;
    - Assumptions, extrapolations and policy judgments;
    - Plausible alternatives and related impacts; and
    - Major risk conclusions and degree of confidence based on uncertainties.
- Outline a process of stakeholder engagement, including
    - An interactive "problem formulation" at the outset of each assessment to identify key issues and data needs;
    - Timing assessments to make maximum use of relevant external research; and
    - Outreach regarding proposed charge questions for peer review of the assessment.
- Consider how the concept of proportionality can be addressed in risk assessment standards, so that risk assessments are more closely linked to the decision they are used to justify.

There are a number of options by which these standards can be developed and appropriate oversight of Agency adherence to the standards established.[5] For example, if the Environmental Research, Development and Demonstration Authorization Act (ERDDA) is reauthorized, Congress can direct EPA to develop and implement these standards.

Congress could also consider a mandate that federal agencies collaborate in an interagency committee that would be tasked with developing risk assessment standards that all agencies would have to follow. This might include standards outlining the basic assumptions underlying risk assessment methodologies (such as concepts of threshold versus linear modeling), the use of animal data, and weight of the evidence approaches. The logic behind this approach is that it could bring together the agencies charged with balancing competing risks and benefits from protective interventions (e.g., the Food and Drug Administration, the Centers for Disease Control), with those agencies whose mandates are to reduce risks (e.g., EPA and the National Toxicology Program). The critical point, of course, is to avoid the development of lowest common denominator standards that simply preserve the status quo.

Congress could also direct the practice of federal agency risk assessment across the federal government by requiring the Office of Management and Budget (OMB) and the Office of Science and Technology Policy (OSTP) to develop standards broadly applicable across the government. Both OMB and OSTP have career staff knowledgeable about risk assessment and are interested in improving agency estimates of risks. In 2006, OMB and OSTP issued a proposed bulletin providing guidance to federal agencies regarding their conduct of health, safety and environmental assessments.[6] Ultimately, OMB reinforced existing guidance, and noted an expectation that agencies would follow the principles. Unfortunately, agencies appear to routinely ignore these principles. Upper and lower bound estimates are not provided, negative studies are not discussed, and the uncertainties and limitations of the assessment are not articulated. Congress should ensure that agencies follow these basic principles.

[5] These proposals do not address who is responsible for generating the data that is used in these assessments. ACC assumes that companies will typically have that responsibility.
[6] *See* 71 Fed. Reg. 2600 (Jan. 17, 2006).

II. Improving the Quality of Science Through Enhanced Peer Review

Integrating scientific methods across EPA and the Federal agencies also requires enhancing the manner in which the broader scientific community is engaged in the assessment process. In ACC's view, the standards governing scientific peer reviews should be updated to make this vital process more effective. Peer engagement and review are two critical factors in the effort to ensure high quality, reliable science supports decision-making. Although ACC focuses on EPA in this section, the recommendations we provide should inform enhanced peer review across the government.

Independent peer review is a critical element of EPA's scientific policies and practices, and to date has received less attention than other elements of IRIS. Peer review is defined by EPA as "an in-depth assessment of the assumptions, calculations, extrapolations, alternate interpretations, methodology, acceptance criteria, and conclusions pertaining to the specific major scientific and/or technical work product and of the documentation that supports them."[7] Peer review plays a crucial role in development of the best scientific evaluation and is integral to identifying information that would reduce uncertainty in significant areas of the assessment. The process of peer review should be structured to accomplish these objectives. There are several areas to consider for enhancing EPA's peer review process:

- Peer review panels need to have sufficient time and resources to fulfill their responsibilities.
- Rather than base peer review charge questions solely on the input provided by the lead agency office, the preparation of these charge questions should reflect stakeholder input and be developed using an iterative process. Development of the charge questions should be initiated at the problem formulation step, and then issued as a refined draft coinciding with the release of the draft IRIS assessment. Public comments on the draft charge questions should be solicited.
- Peer review charge questions should be written in order to facilitate objective consideration of alternative plausible scientific views rather than from the vantage point of giving deference to the interpretation presented in the Agency assessment. This provides peer reviewers greater opportunity to consider alternative scientific views such as those offered by stakeholders.
- As recommended in the Bipartisan Policy Center's report "Improving the Use of Science in Regulatory Policy," EPA should "explicitly differentiate between questions that involve scientific judgments and questions that involve judgments about economics, ethics and other matters of policy."[8]
- Peer review meetings should be structured to encourage open scientific dialogue and thoughtful scientific deliberation. Stakeholder input should not be limited to a few minutes at the beginning of a meeting; greater effort should be made to structure the

[7] U.S. Environmental Protection Agency, Peer Review Handbook 3rd Edition, EPA/100/B-06/002, at 12. Available at http://www.epa.gov/peerreview/pdfs/peer_review_handbook_2006.pdf.

[8] The Center's report is available at http://www.bipartisanpolicy.org/sites/default/files/BPC%20Science%20Report%20fnl.pdf.

meetings so that stakeholder input is provided and deliberated at strategic times throughout the meeting. Moreover, peer reviewers should not be dissuaded from embarking on open technical discussion/ scientific exchange with stakeholders.

- In selecting peer review panel members, the foremost consideration should be given to expertise. Qualified scientists from industry should be given equal consideration for appointment based on the subject matter, and in accordance with applicable conflict of interest provisions. There is unanimity among the most authoritative sources on this point, including the National Academies of Science and the Society of Toxicology:

> Appointments to scientific advisory bodies should be based principally on the scientific credentials, demonstrated accomplishments, and professional credibility of the nominee. His/her source of employment and funding (past or present), religious beliefs, political persuasion, sexual orientation, gender, or race/ethnicity should not be used as (a) determinant(s) of exclusion to such a scientific advisory body.[9]

The Office of Government Ethics (OGE) has issued detailed rules under the Ethics in Government Act (EGA) and the federal criminal code addressing conflict of interest, and impartiality, on the part of government employees, including "Special Government Employees" serving part-time on peer review committees. Fairly interpreted, the EGA and those rules strike a fair balance and allow persons employed by industry or non-governmental organizations to serve as reviewers in many cases. However, agencies have tended to interpret these rules in ways that (i) restrict the participation of industry personnel and (ii) are too accepting of persons who are not really independent of the agency or the work being reviewed. Congress may wish to revisit the EGA and the rules, and their role in promoting high quality, reliable science.

In ACC's view, EPA's Science Advisory Board (SAB) has adopted generally sound processes and criteria for peer review of Agency action. There is room for improvement, however. For example, the SAB should ensure that the SAB peer reviewers fully understand their independent roles as peer reviewers. At times, however, it appears that peer reviewers are overly deferential to EPA, reluctant to be seen as criticizing EPA staff. It also appears that EPA staff have an unfettered ability to comment throughout the peer review meetings, and their constant presence may have a chilling effect on frank and open discussion among the peer reviewers. This practice contrasts sharply with NAS peer reviews.

ACC is generally encouraged by EPA's recent announcement that it will establish a standing SAB panel for IRIS assessments. Assuming that that standing panel is truly independent, and the panel process addresses the concerns such as the role of EPA staff and how review comments are incorporated into completed IRIS assessments, this approach could help promote a more reliable and consistent IRIS process.

Responding to peer review and public comments is another area where the Agency needs to make improvements in its practices. It is imperative that the Agency provide a robust response in writing to comments as part of the assessment revision process that follows the public

[9] *See* Society of Toxicology, Appointment and Participation of Scientists on Peer Review Panels and Scientific Advisory Boards, available at http://www.toxicology.org/pm/AdvisoryBoard.asp.

comment and peer review phases. Where the Agency elects not to address a peer review finding or recommendation, or a significant public comment, EPA should provide a written justification. This practice should be made routine for all federal agencies.

The current practice of having the same office that develops the assessment draft the charge questions, review public and peer review comments, decide which recommendations and findings to act on and which to ignore, and develop the final assessment is clearly not a best practice. The inherent value of peer review – indeed the inherent value of EPA's SAB – is to provide an objective, robust scientific review of the agency's scientific work product. ACC believes there is value in having an "honest broker" to oversee and ensure that the Agency adequately revises assessments in a manner that addresses both public comments and the findings and recommendations of independent scientific peer review. At this time, upon receiving a SAB or NAS panel report, EPA unilaterally decides what elements to accept or reject – a practice that clearly has not worked, particularly given the NAS report on formaldehyde. Reviewing bodies should have an opportunity to address how the Agency intends to implement the recommendations.

III. Improving the Quality of Science by Leveraging Emerging Science and Technology

One of ACC's key objectives is to ensure that federal risk assessment policies and practices rely on 21st century knowledge of toxicology, biological modes of action, and advanced mechanistic technologies. There are dramatic changes underway in the science and technology of assessing chemical risks. These changes promise a revolution in the speed and accuracy with which chemical hazards, exposures and risks are evaluated and managed.

While EPA has made important investments in developing new, highly reliable technologies that can speed chemical assessments, not all offices within EPA appear disposed to adopt these technologies when appropriate. Successful integration of emerging science and technology into risk assessment will require a concerted and methodic approach to evaluate the science and build consensus around their readiness.

The field of toxicology has grown more sophisticated as we have learned more about the biochemical mechanisms of toxicity and the differences between humans and test animals. New and exciting technologies for evaluating chemicals are emerging. In some cases, however, agencies are not well prepared to implement these new tools. Many Federal agencies still cling to a set of conservative default assumptions little changed from the 1960s and 70s, and appear to be reluctant to adopt new technologies.

In ACC's view, it is critical that the Federal government and the chemical industry be actively engaged in the transformation of chemical safety sciences. ACC member companies have made a significant, continuing investment in the ACC Long-range Research Initiative (LRI) to inform

and advance this objective. ACC currently commits some $5 million annually[10] to the program, which is designed to help:

- Drive development of innovative approaches to assess and interpret health risks from low-dose exposures to chemicals and exposures to mixtures.
- Develop and apply new tools to interpret the explosion of biomonitoring and high-throughput testing data regarding human health risks.
- Accelerate the shift away from traditional high-dose animal toxicological testing by developing, validating, and promoting broad acceptance of approaches with greater relevance for humans.
- Translate emerging research outcomes for decisions about the safety of our chemicals by partnering with thought leaders from industry, government, academia, and public interest groups.

The LRI program's hallmark is the collaborative work to catalyze technological innovations in chemical safety sciences with the Federal government, principally EPA and the National Institutes of Health. Examples of current collaborations between industry and governmental agencies include several ongoing projects between the Hamner Institute for Health Sciences and the EPA's National Center for Computational Toxicology (NCCT) and its National Center for Environmental Assessment (NCEA).

Other collaborative projects funded by the LRI extend ongoing work at the National Institute of Environmental Health Sciences (NIEHS). The unprecedented collaborations that the LRI has fostered among industry, governmental and regulatory agencies, and academia and demonstrates how an industry-sponsored initiative can effectively partner with other stakeholders to provide knowledge for science-informed decisions.

Among the collaborative research supported by the LRI program:

- Efforts to deliver state-of-the-art exposure science to advance the ExpoCast™ component of EPA's ToxCast™ program.
- Advance the interpretation of high-throughput data.
- Accelerate the paradigm shift in chemical risk assessment by incorporating ToxCast™ data and toxicogenomics information into EPA's NexGen Risk Assessment program.
- Support validation of innovative biomarkers of cumulative exposures.
- Promote development of alternatives to animal testing.

The LRI program adheres to a stringent set of principles designed to ensure that the collaborative research we fund meets the highest standards for scientific excellence, transparency, and fairness.

[10] ACC estimates that as a whole, the business of chemistry spent some $55 billion on research and development in 2010, the last year for which complete data are available. Slightly over 40% of that amount was spent on basic and applied research.

The LRI program is focused not only on the new technologies for toxicological testing that are revolutionizing risk-based decision-making, but is also helping to develop innovative biologically-relevant approaches to understanding exposure. These technologies present an opportunity to develop a new paradigm for toxicity testing of chemicals, facilitate understanding of chemical hazards, and improve chemical safety evaluations. The current problem that they present is the growing gap between the advancements in these new technologies and the science to interpret and understand the emerging data.

In addition to providing state-of-the-art science and technology for chemical safety and risk assessments, LRI promotes development of tools that can be used by chemical companies for product innovation. For example, the LRI currently manages one of the most comprehensive portfolios of exposure projects that relate directly into efforts to a) predictively develop exposure information, and b) make existing exposure data widely available. Without these tools and data, there would be an increased likelihood that the next generation of risk assessments would be based entirely on hazard information or on overly-conservative exposure assumptions.

ACC has suggested to EPA that the transition to new integrative and predictive molecular and computational techniques can be enhanced by focusing on critical issues such as:

- The need for an improved understanding of what short-timescale *in vitro* assays can foretell about the likelihood of long-timescale processes that lead to *in vivo* toxicity endpoints.[11] For example, specific response profiles in certain *in vitro* assays or combinations of assays could provide insights into potential toxicity endpoints, such as cancer, and may be useful in such decisions as prioritizing chemicals for additional testing. Considerable work is underway to enhance confidence in the use of these approaches and better interpret the results.
- The value of increased collaboration and engagement across the scientific community to interpret ToxCast data for chemical prioritization. Increased transparency of relevant data and algorithms will allow EPA to leverage its intellectual resources and garner stronger understanding of and support for its approaches. EPA's NexGen Risk Assessment process already provides a similar mechanism to engage experts and stakeholders in the emerging science.

Conclusion

Ensuring that EPA decision making is firmly based on the use of high quality science is critical to helping the Agency meet its obligation to protect human health and the environment. This can be achieved by common sense reforms that will lead to more efficient and effective regulatory decisions. ACC looks forward to working with members of the Subcommittee to ensure that the science and processes that support the important regulatory work of the Federal government meet the highest standards for quality and reliability.

[11] Judson, R., et al., *In Vitro* Screening of Environmental Chemicals for Targeted Testing Prioritization: The ToxCast Project, *Environmental Health Perspectives* 118:485–492 (2010).