



**Written Statement of
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**Before the
U.S. House of Representatives
Committee on Science, Space, and Technology
Subcommittee on Oversight and Subcommittee on
Environment**

**Regarding a Hearing on
“Status of Reforms to EPA’s Integrated Risk Information
System”**

July 16, 2014

I. Federal Chemical Assessment Programs Must be Scientifically Based

On behalf of the members of the American Chemistry Council (ACC),¹ I very much appreciate the opportunity to appear today to discuss an area that has important implications about the role of science in regulatory decision-making.

ACC and its member companies care deeply about how scientific information is used, evaluated, and disseminated by the Environmental Protection Agency (EPA) and other federal agencies.

Federal chemical assessments focus on understanding the inherent properties of substances in order to determine the likelihood of harm from a specific exposure. The public, businesses, and regulators at all levels of government look to these assessments as a reliable source of information about the potential hazards and risks associated with chemicals.

The outputs of federal assessments are a critical part of the decision-making process for chemical management regulatory programs (e.g., Toxic Substances Control Act) and environmental regulations (e.g., Clean Air Act). Access to accurate and useful data regarding potential hazards and risks is necessary in order for these programs to effectively protect human health and the environment, as well as provide for the development and use of chemicals that are vital to everyday life.

According to recent reports and studies, the scientific foundation underpinning these programs must be improved to ensure agencies produce timely and credible assessments.

Objective scientific analysis and transparency must be at the core of how the federal government evaluates the safety of chemicals. Flawed assessments can contribute to a lack of confidence in federal and state chemical management programs and environmental regulations, all of which routinely rely on the assessments. They can also create public confusion and unwarranted alarm and may lead to unnecessary cost, product de-selection, and litigation, which ultimately can have negative economic impacts without sound scientific basis. Moreover, these shortcomings may have further significant unwarranted economic impacts, because risk management decisions throughout the federal government, as well as state governments, routinely draw upon the risk numbers contained in the assessments.

ACC believes that the federal government must apply a more advanced scientific approach to chemical hazard and risk assessments. We have serious concerns that without additional changes, the federal government's policies and practices will continue to perpetuate the development of unrealistic overestimates of risks.

¹ The American Chemistry Council represents over 160 member companies in the \$812 billion enterprise that is American chemistry. With continued access to abundant supplies of natural gas from shale deposits, the industry's competitive edge has been substantially enhanced, and the United States is now one of the most attractive places in the world to invest in chemical manufacturing. ACC estimates that over \$117 billion will be invested in American chemistry between now and 2020, adding to the \$35 billion invested in 2013 alone. More than 96 percent of all manufactured goods are touched directly by the business of chemistry, which provides over 790,000 domestic jobs and accounts for 12 percent of U.S. exports.

ACC recently released a set of comprehensive chemical hazard and risk assessment principles² that outlines a series of attainable, high-level benchmarks for modernizing federal chemical hazard and risk assessment programs. A copy of our principles is attached to this testimony. Our principles outline four key areas for improvement: 1) the design of assessments; 2) the data and methods used in assessments, importantly including how scientific evidence is judged and integrated; 3) the communication of assessments; and 4) review and accountability. These principles are relevant to all federal chemical hazard and risk assessment programs (such as NIEHS's Report on Carcinogens, ATSDR's Toxicological Profiles, and EPA's TSCA work plan assessment program), not just the IRIS program.

II. The NAS Has Outlined a Series of Recommendations for Improvements in the IRIS Program

In 2011, the National Academy of Sciences (NAS) review of EPA's draft formaldehyde IRIS assessment included an entire chapter³ that addressed concerns about the scientific shortcomings across the IRIS program. The NAS report was, in ACC's view, a tipping point for bringing much-needed attention and oversight to the IRIS program. EPA has committed to implementing these recommendations.⁴

Three years after that report was released, however, many of the most critical changes needed to achieve the scientific standards articulated in the 2011 NAS recommendations have not been fully implemented. In fact, just last week,⁵ EPA indicated that it expects to fully implement the 2011 NAS recommendations in only two chemical assessments in the IRIS queue.

Six weeks ago, the NAS released a second report⁶ that demonstrates EPA has much work to do to ensure that the IRIS program is effective and efficient. The 2014 report reiterated many of the same concerns noted in the 2011 report and provided further recommendations for improvement, particularly in the area of systematic review. Although the 2014 report does note several areas of improvement, the unfortunate fact is that not a single IRIS assessment, either draft or final, implements all the NAS recommendations.

EPA has made important progress in addressing some of the concerns raised by the 2011 NAS report. Dr. Ken Olden has provided important leadership in driving the IRIS program to achieve a higher standard of public engagement, transparency, and openness. Dr. Olden has taken steps that, when fully implemented, will allow for substantive discussion with stakeholders even before the draft assessment is released.

For example, Dr. Olden has initiated a series of bi-monthly meetings in which EPA actively seeks input from stakeholders to address problem formulation and to discuss important scientific issues. It is our hope that these early discussions will lead to scientifically robust draft

² See <http://www.americanchemistry.com/Media/PressReleasesTranscripts/ACC-news-releases/ACC-Announces-New-Principles-to-Enhance-Chemical-Hazard-and-Risk-Assessments.html>.

³ See http://www.nap.edu/catalog.php?record_id=13142.

⁴ See <http://www.epa.gov/iris/pdfs/irisprogressreport2012.pdf>.

⁵ See

[http://yosemite.epa.gov/sab/sabproduct.nsf/C50769FFFA37E22B85257D0F0057E2AB/\\$File/PDF+of+Ammonia+panel+presentation.PEROVICH.07.07.pdf](http://yosemite.epa.gov/sab/sabproduct.nsf/C50769FFFA37E22B85257D0F0057E2AB/$File/PDF+of+Ammonia+panel+presentation.PEROVICH.07.07.pdf) at slide 9.

⁶ See National Academy of Sciences, Review of EPA's Integrated Risk Information (IRIS) Process, http://www.nap.edu/catalog.php?record_id=18764.

assessments that more accurately reflect up-to-date knowledge of modes of action and hazards and risks at environmentally relevant levels of exposure.

III. IRIS Reforms Must Continue

The most critical area for IRIS reform – evaluating and integrating scientific evidence in a transparent and robust manner – remains to be achieved. For instance, the IRIS program has identified some study quality considerations for certain types of scientific evidence, but assessments have not systematically and transparently evaluated each of the studies against these considerations.

EPA must also develop and use pre-defined, objective criteria to evaluate the quality and relevance of all studies (animal, human, and mechanistic) in a transparent manner. The NAS recommended this in 2011 and again stressed the importance of study quality evaluations in its 2014 report. Other programs, such as EPA's High Production Volume Challenge Program and Office of Pesticides Program, as well as the Organisation for Economic Co-operation and Development, have routinely used such criteria for evaluating animal toxicity studies for many years.

Criteria have also been published in the peer reviewed scientific literature for evaluating *in vitro* studies and human epidemiological studies for quality and reliability. EPA has not articulated a rationale for not adopting and implementing these readily available approaches.

The availability of defined criteria is a critical early step to ensure that all studies are not simply treated as being of equal quality. With pre-defined, objective criteria, EPA can comprehensively review, give appropriate weight to, and integrate into its assessments data from laboratory experiments, epidemiological investigations, and cutting-edge mechanistic research from all relevant studies (including those that comport with Good Laboratory Practice [GLP] and those that do not) from all investigators, regardless of affiliation or funding source. Done correctly, this will ensure that the IRIS program gives more weight to results of the most relevant and highest quality studies than results from poorer quality and less relevant studies.

Having pre-defined criteria for including and excluding studies is a critical component of any systematic review. Although EPA has been more transparent in defining search criteria for studies to ensure key investigations are not missed, comparable progress in evaluating study quality, including internal and external validity, has not been made.

EPA's approaches to integrating evidence have left stakeholders guessing as to how mode of action, which relates to how the human body works and the way chemicals interact with the body at different levels of exposure, and mechanistic information will be used. In order to modernize IRIS assessments so that they use all available and relevant high-quality information, EPA needs to consistently address mode of action. By designing IRIS assessments from the start to fully integrate current knowledge on mode of action, the Agency can organize the available data to objectively evaluate all plausible alternative hypotheses that may be supported by the data.

For example, independent researchers supported by ACC's hexavalent chromium panel recently completed a multimillion dollar scientific research program focused on characterizing the mode of action (following EPA's guidelines) for hexavalent chromium. These research

results ensure that, in lieu of unrealistic default assumptions, solid scientific data is available for use in IRIS and other federal and state program assessments. With these data, EPA can develop a more accurate and realistic assessment of the potential risks to humans at environmental levels of exposure.

This extensive research made use of cutting-edge science from over a dozen research organizations, the insights of an external peer review panel for the research protocol and major findings, and culminated in more than a dozen scientific articles published in leading peer reviewed journals. ACC is concerned that, despite the new science with its multiple peer review steps, EPA may continue to inappropriately give greater weight to default cancer risk assessment approaches that are based on a 1970s understanding of the processes of carcinogenesis.

For example, in 2011 the NAS admonished the Agency for failing to embrace solid scientific research on biologically based dose-response (BBDR) modeling in its draft formaldehyde assessment. The NAS noted that EPA's "manipulations are extreme, may not be scientifically justified, and should not have been used as the basis of rejection of the use of the BBDR model in its assessment."

In our view, EPA's assessment of hexavalent chromium will be a critical litmus test. If EPA objectively evaluates and fully uses the mode of action data, then the Agency will signal a true commitment to implement both the NAS recommendations and its own more recent guidelines.

It would also be helpful if EPA could better articulate, in advance of conducting assessments, the standards for using data rather than assumptions and scientific information rather than defaults. To comprehensively evaluate the potential toxicity and risks of a substance, EPA should evaluate multiple alternative hypotheses to see which ones are best supported by the available data, and present central estimates, not just upper bounds, consistent with the recommendations in the 2014 NAS report.

The IRIS program has begun to draft an IRIS Handbook to provide a roadmap for implementation of the 2011 NAS recommendations. The draft Handbook is not yet complete, and as EPA has acknowledged, several pieces are missing. The missing elements include:

- Integrating evidence (epidemiological, toxicological, and mechanistic data) to identify hazards and transition to dose-response analysis;
- Conducting dose-response modeling;
- Extrapolating to lower doses and response levels;
- Considering susceptible populations and lifestyles;
- Developing candidate toxicity values;
- Characterizing confidence and uncertainty in toxicity values; and
- Selecting final toxicity values.⁷

The 2014 NAS report is silent on many of these important topics, as the Agency was not yet ready to provide drafts on these elements. The 2014 NAS panel also noted the need for peer

⁷ See EPA Jan 30, 2013, Part 1: Status of Implementation of Recommendations, http://www.epa.gov/IRIS/pdfs/IRIS%20Program%20Materials%20to%20NRC_Part%201.pdf, at page F-1.

review before making the Handbook final. ACC agrees with that suggestion. In addition, EPA needs to engage stakeholders as it works to update and complete the draft IRIS Handbook. Many pieces of the current draft Handbook, such as the development of a causality framework for non-cancer endpoints, need significant re-tooling. IRIS assessments will benefit greatly if the program engages stakeholders early in the development process.

Peer review in the IRIS program also needs to be enhanced. While the Chemical Assessment Advisory Committee (CAAC) is a helpful development, EPA also needs to ensure that this panel, or a similar independent panel, is used to review IRIS guidance. The CAAC should be engaged not only on chemical specific reviews, but also in evaluating cross-cutting scientific issues that can impact multiple assessments.

As EPA's Science Advisory Board (SAB) and Board of Scientific Counselors (BOSC) have recommended, strategies should be developed to more efficiently address peer review comments.⁸ The joint SAB and BOSC report notes the NAS example of an independent review monitor to provide critical guidance on addressing comments. Similar to the role of a journal editor, the NAS review monitor helps to ensure that comments from reviewers have been appropriately and sufficiently addressed.

Currently, the IRIS process lacks an independent review monitor. Instead, EPA staff (the authors of the draft assessments) have full discretion to determine which peer review and stakeholder comments will be the subject of a response. EPA staff also determine if the Agency's response is sufficient. Further improvements are necessary in this area and should be incorporated into the IRIS Handbook.

An important area not addressed in the draft Handbook or by the NAS is how the IRIS program prioritizes its resources and the list of chemicals that will be evaluated. Considering the efforts involved in completing an IRIS assessment, ACC believes the program should focus on those chemicals with robust scientific databases, significant uses, and potential exposures. Most importantly, the program needs to provide a clearly articulated rationale for assessing substances. Determining priorities is an area where the IRIS program could benefit from further input and dialogue with stakeholders.

Finally, how risk information is characterized and communicated to the public is critically important. When assumptions are used in lieu of data, the assumptions must be disclosed along with the justification for their use. The final characterization of hazards and risks should provide a complete picture of what is known and what has been inferred and should present results based on alternative plausible assumptions. The 2014 NAS report noted the importance of developing guidelines for uncertainty analysis and communication. The NAS also recommended improving the way EPA presents dose-response estimates, in particular calling for the presentation of two estimates, including a central estimate. Presentation of both the central estimate and upper bound should commence today and should be included in every draft and final IRIS assessment henceforth, as such calculations are readily derived. We look forward to seeing these and other recommendations implemented within the IRIS program.

⁸ See Sept 28, 2012, report, [http://yosemite.epa.gov/sab/sabproduct.nsf/3822EB089FCCB18D85257A8700800679/\\$File/EPA-SAB-12-012-unsigned.pdf](http://yosemite.epa.gov/sab/sabproduct.nsf/3822EB089FCCB18D85257A8700800679/$File/EPA-SAB-12-012-unsigned.pdf).

ACC appreciates the opportunity to comment on developments in the IRIS program. We look forward to working with EPA and Congress to ensure that federal chemical assessments meet appropriate standards for quality, reliability, and confidence.

Principles for Improving Federal Chemical Hazard and Risk Assessment Programs



Federal assessments of chemical hazards and risks are a key component to establishing a successful regulatory system. Assessments focus on understanding the inherent properties of substances in order to determine the likelihood of harm from a specific exposure. The public, businesses, and regulators at all levels of government look to these assessments as a reliable source of information about the potential hazards and risks associated with chemicals.

The determinations from assessments are a critical part of the decision-making process for chemical management regulatory programs (e.g., Toxic Substances Control Act) and environmental regulations (e.g., Clean Air Act). Access to accurate and useful data regarding potential hazards and risks is necessary in order for these programs to effectively protect human health and the environment, as well as provide for the development and use of chemicals that are vital to everyday life.

Unfortunately, too many assessments fail to consistently meet the benchmarks of objectivity, transparency, and scientific accuracy. Delays often arise as a result of the need to address shortcomings in draft assessments. Furthermore, flawed assessments may create public confusion, stir unwarranted alarm, and lead to unnecessary regulatory actions, product de-selection, and litigation. All of which only serve to further erode public confidence in chemical management programs.

Given the central role assessments have in regulatory decision making and to ensure that regulatory actions on chemical substances are based on a firm scientific foundation, the U.S. government should incorporate the following principles into chemical assessment programs:

DESIGN

- 1. ENSURE KEY ISSUES ARE IDENTIFIED PRIOR TO INITIATION OF THE ASSESSMENT:** The purpose, scope, and technical approaches that will be used in assessments need to be delineated as part of the design process. Assessments should be tailored to meet the intended purpose, and stakeholders should be engaged during problem formulation. As agencies develop or revise guidance for hazard and risk assessment programs, stakeholders should have the opportunity to provide input as drafts are developed. Draft guidance should be submitted for public comment and peer review.
- 2. UTILIZE MODERN SCIENTIFIC INFORMATION AND TOOLS RATHER THAN CONTINUING TO RELY ON OUTDATED ASSUMPTIONS:** Reliance on defaults should be minimized. In many cases, government hazard and risk assessment programs rely on assumptions and default approaches developed in the 1970s. Today's scientists and health professionals have a wealth of knowledge including 21st-century understanding of how the human body works and the way chemicals interact with the body and the environment at different levels of exposure. This modern-day knowledge must be applied when determining chemical safety.



DATA & METHODS

- 3. INTEGRATE STUDIES TO ASSESS THE OVERALL WEIGHT OF THE EVIDENCE:** Assessments must rely on the best available scientific information, and they must employ consistent, objective methods and models to derive realistic determinations of hazards and risks at environmentally relevant levels of exposure. Scientifically valid, up-to-date data and knowledge of possible hazards and risks of substances should be used. All assessments must be based on a framework that takes into account - and integrates - all relevant studies, while giving the greatest weight to information from the most relevant and highest quality studies.
- 4. DEVELOP AND APPLY CONSISTENT CRITERIA FOR EVALUATING DATA AND FOR SELECTING STUDIES USED IN ASSESSMENTS:** Transparent criteria must be established upfront and then consistently applied throughout the assessment to identify studies and to evaluate their quality, relevance, and reliability.



COMMUNICATION

- 5. ENSURE ASSESSMENTS ARE TRANSPARENT:** Agencies must disclose key information used to develop assessments. When assumptions are used in lieu of data, the assumptions must be disclosed along with the justification for their use. The impact of each assumption on the evaluation should be clearly stated. Publicly available electronic dockets should be used to capture all materials, including supporting documentation, as assessments go through the development and public comment process.
- 6. CHARACTERIZE HAZARDS AND RISKS FULLY AND ACCURATELY:** Hazards and risks must be objectively characterized and presented in a manner understandable to stakeholders and risk managers. The characterization should provide a full picture of what is known and what has been inferred and should also present results based on alternative plausible assumptions. When a screening level assessment indicates potential concern, prior to initiating additional risk management actions, a refined assessment should be conducted to more accurately determine hazards or risks. When going beyond screening level, assessments should include central estimates and ranges; it is not sufficient to rely on theoretical maximum exposure estimates to characterize potential risks.



REVIEW & ACCOUNTABILITY

- 7. ENHANCE SCIENTIFIC PEER REVIEW AND RESPONSIVENESS:** Assessments must be subject to appropriate review by independent experts based on the importance and complexity of the decision. Peer reviewers must be fully independent from the program issuing the assessment. Peer review panels should be assembled in accordance with appropriate policies to ensure the range of technical expertise required is achieved, perspectives are balanced, and potential financial conflicts of interest are rigorously and fairly evaluated.
- 8. IMPROVE ACCOUNTABILITY:** Processes need to be in place to ensure that public comments and peer review findings and recommendations are completely addressed and that legitimate scientific concerns are not disregarded. An independent accountability procedure should be implemented to verify that revised assessments are accurate, that they are fully responsive to comments and peer review recommendations, and that the necessary scientific and process improvements are embodied in specific chemical assessments.