Written Statement of
Nancy B. Beck, Ph.D., DABT
Senior Director of Regulatory & Technical Affairs
American Chemistry Council

Before the
U.S. Senate Committee on Homeland Security and Governmental Affairs
Subcommittee on Regulatory Affairs and Federal Management
Regarding a Hearing on the Agency Use of Science in the Rulemaking Process:
Proposals for Improving Transparency and Accountability

March 9, 2017

American Chemistry Council
700 2nd Street, N.E.
Washington, D.C. 20002

Summary

The American Chemistry Council (ACC)[1] appreciates this opportunity to provide testimony on Federal Agency use of science in the rulemaking process, and particularly on proposals for improving transparency and accountability.

The business of chemistry is a critical component for manufacturing safe, high quality products and 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. Similarly, they expect high quality, up to date science and relevant reliable assessment processes to underpin regulatory decisions by the Federal government.

Reliance on the highest quality, best available science is critical to ensuring public trust. Without it, consumers are at a severe disadvantage. Stakeholders can lose confidence in regulatory decision making, which in turn can lead to product de-selection that is not supported by science, unwarranted public alarm and unnecessary costs.

ACC supports actions to enhance the integration of the best available scientific knowledge and weight of the evidence methods as the foundation for regulatory decision making across Federal Agencies. We also support improving the technical quality and objectivity of Agency evaluations, particularly through enhancing the transparency of how the science is being considered, interpreted, and evaluated.

In 2002, Federal Agencies were directed to ensure the quality, objectivity, utility and integrity of information which they disseminated to the public.[2] In theory, this should have had a direct impact on improving the quality of scientific analyses that support regulatory decisions. Unfortunately, while most Agencies have committed to meeting these standards, we have seen that some of the scientific analyses that have come out of the EPA and other Federal Agencies fall short of meeting the objectivity and quality standards discussed in the government-wide Information Quality Guidelines.

[1] 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 $797 billion enterprise and a key element of the nation's economy. It is the nation's largest exporter, accounting for fourteen percent of all U.S. exports. It is also one of the nation's most heavily regulated industries. Chemistry companies are among the largest investors in research and development.

[2] Pursuant to what is commonly referred to as the Information Quality Act (Sec. 515 of the Treasury and General Government Appropriations Act for FY 2001, Pub. L. No. 106-554), the Office of Management and Budget (OMB) issued government-wide Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies (2002), 67 Fed. Reg. 8452 (Feb. 22, 2002) [hereinafter Information Quality Guidelines], available at: https://georgewbush-whitehouse.archives.gov/omb/memoranda/fy2007/m07-24.pdf;

ACC's testimony today discusses some of the standards that already exist, discusses the new Lautenberg Chemical Safety Act scientific standards, and provides some suggestions for ensuring the quality of science that supports regulatory activities. We also share examples of where some Agencies' scientific evaluations continue to fall short.

I. The Need for Confidence in Science

As we are all aware from the news media, there is a large public perception that science may not inform Federal Agency decision making. Indeed even organizations like the American Association for the Advancement of Science (AAAS) have now become official partners in the planned April 22, 2017 March for Science. Dr. Rush Holt, the CEO of AAAS has stated "We see the activities collectively known as the March as a unique opportunity to communicate the importance, value and beauty of science."[3] Concerns about confidence in science, particularly to inform regulations, is not new and certainly did not begin with the 2016 elections.

In 2013, George Mason University conducted a survey to help capture the viewpoints of the scientific community on the state of regulatory risk assessment. The survey "Expert Opinion on Regulatory Risk Assessment" reached out to all members of the Society of Toxicology Risk Assessment Specialty Section, the Society for Risk Analysis Dose Response Section and the International Society for Regulatory Toxicology and Pharmacology.[4] The survey focused on how well and how frequently critical parts of a risk evaluation were conducted (e.g., was there a problem formulation, were standardized protocols used for data collection, was a weight of evidence approach used, was peer review sufficient). In general, the findings showed that there is widespread concern over the current application of these procedures and also showed concerns about the amount of attention given to scientific factors in risk management.[5]

In July 2016, almost 200 toxicologists signed "an appeal for the integrity of science in public policy."[6] This appeal urges legislators to embed the "rules of evidence" of the scientific method in statutes governing administrative policy and regulations. These scientists are concerned that precautionary regulations and policies are being presented as objective science, when in reality they are not. In another recent article, Dr. Andrew Rosenberg of the Union of Concerned Scientists stated, "When science is sidelined from policy decisions, we all lose."[7] ACC shares the concerns and recommendations of this diverse set of scientists. Too often we see scientific assessments, or even policies, that are driven by default assumptions rather than actual scientific evidence.[8]

ACC has consistently called upon the EPA to improve the design and conduct of its chemical assessments. In 2014, ACC released Principles for Improving Chemical Hazard and Risk

[3] See Science Magazine, Feb 28, 2017 article available at: http://www.sciencemag.org/news/2017/02/will-they-or-won-t-they-what-science-groups-are-saying-about-joining-march-science.
[4] The Survey and results can be found at: https://cmpa.gmu.edu/wp-content/uploads/2013/12/GMU-Study-Report.pdf.
[5] Ibid at page 2.
[6] See article available at: http://www.sciencedirect.com/science/article/pii/S0300483X16301123.
[7] See Science Magazine, Feb 17, 2017 article available at: http://science.sciencemag.org/content/355/6326/696/tab-pdf.
[8] See NIOSH Carcinogen Policy example provided in Appendix 1 of this testimony.

Assessments.[9] ACC did not invent these principles. For years, authoritative bodies, like the National Academy of Sciences (NAS), have provided similar constructive input to the EPA.[10] Appendix 1 of this testimony provides some specific examples of cases where Federal Agency evaluations have not met scientific standards.

II. Tools and Standards Exist to Improve Agency Science

Improving Federal Agency science should not be as challenging as it has been. Significant governmental and non-governmental guidance already exists. As noted below, often this guidance is not followed.

a. Information Quality Guidelines

In 2002, the Office of Management and Budget (OMB) released the Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies (Information Quality Guidelines).[11] The guidelines were then adopted by Federal Agencies and the OMB's principles were to be reflected in the agency-specific guidelines.

With regard to the analysis of risks to human health, safety and the environment, Agencies have adopted or adapted the quality principles applied by Congress to risk information used and disseminated pursuant to the Safe Drinking Water Act (SDWA) Amendments of 1996 (42 U.S.C. 300g-1(b)(3)(A) & (B)). In these amendments, Congress emphasized that EPA must use the best available scientific evidence for risk information. Since the Information Quality Guidelines directed all Agencies to adopt this standard, Agencies were directed, "to the degree that an Agency action is based on science," to use:

> (i) the best available, peer-reviewed science and supporting studies conducted in accordance with sound and objective scientific practices; and (ii) data collected by accepted methods or best available methods (if the reliability of the method and the nature of the decision justifies use of the data).

Additionally, the 1996 SDWA amendments directed EPA "to ensure that the presentation of information [risk] effects is comprehensive, informative, and understandable." The Information Quality Guidelines adopted this language and directed all Agencies:

> [I]n a document made available to the public in support of a regulation [to] specify, to the extent practicable:[12]

[9] See ACC principles available at: https://www.americanchemistry.com/Chemical-Hazard-and-Risk-Assessments-Principles/ and further details at: https://www.americanchemistry.com/Policy/Chemical-Safety/Chemical-Assessments/Principles.pdf.

[10] See for instance chapter 7 in the 2011 NAS Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde available at: https://www.nap.edu/catalog/13142/review-of-the-environmental-protection-agencys-draft-iris-assessment-of-formaldehyde.

[11] The Information Quality Guidelines are available at: https://georgewbush-whitehouse.archives.gov/omb/memoranda/fy2007/m07-24.pdf.

[12] Bracketed language reflects changes to text for clarity.

(i) each population addressed by any estimate [of applicable risk effects];
(ii) the expected risk or central estimate of risk for the specific populations [affected];
(iii) each appropriate upper-bound or lower-bound estimate of risk;
(iv) each significant uncertainty identified in the process of the assessment of [risk] effects and the studies that would assist in resolving the uncertainty; and
(v) peer-reviewed studies known to the [agency] that support, are directly relevant to, or fail to support any estimate of [risk] effects and the methodology used to reconcile inconsistencies in the scientific data.

b. Memorandum on Updated Principles for Risk Analysis

In 2007, OMB and the Office of Science and Technology Policy (OSTP) issued a joint memorandum to Executive Departments and Agencies on Updated Principles for Risk Analysis (Principles for Risk Analysis).[13] This memorandum was intended to reinforce the principles developed in 1995. While the focus was on actions directed at improving public health, safety, and the environment, it was noted that many of the principles were relevant to other fields, such as financial or information technology risk analyses.

The Principles for Risk Analysis reiterated the requirements for best available science as they were articulated in the Information Quality Guidelines and presented further important information regarding the use of and presentation of assumptions, judgments, and uncertainties in risk analyses. For instance, among other requirements, the Principles for Risk Analysis require that:

> Judgments used in developing a risk assessment, such as assumptions, defaults, and uncertainties, should be stated explicitly. The rationale for these judgments and their influence on the risk assessment should be articulated.[14]
>
> Results based on different effects and/or different studies should be presented to convey how the choice of effect and/or study influences the analysis. The presentation of information regarding different scientifically plausible endpoints should allow for a robust discussion of the available data, associated uncertainties, and underlying science.[15]
>
> Due to the inherent uncertainties associated with estimates of risk, presentation of a single estimate may be misleading and provide a false sense of precision. Expert panels agree that when a quantitative characterization of risk is provided, a range of plausible risk estimates should be provided.[16]

[13] See: https://georgewbush-whitehouse.archives.gov/omb/memoranda/fy2007/m07-24.pdf.
[14] Ibid, at page 8.
[15] Ibid, at page 8.
[16] Ibid, at page 6.

c. Non-Governmental Reports on Improving Science in Regulations

Improving Peer Review:

In addition to government guidance, other consensus groups have spoken to the needs for ensuring high quality science. For instance, in 2009 the Bipartisan Policy Center put out a report entitled "Improving the Use of Science in Regulatory Policy."[17] Important recommendations in this report included:

> The Administration needs to promulgate guidelines (through executive orders or other instruments) to ensure that when federal agencies are developing regulatory policies, they explicitly differentiate, to the extent possible, between questions that involve scientific judgments and questions that involve judgments about economics, ethics and other matters of policy.[18]
>
> The federal government, universities, scientific journals and scientists themselves can help improve the use of science in the regulatory process by strengthening peer review, expanding the information available about scientific studies, and setting and enforcing clear standards governing conflict of interest.[19]

In 2012, the Keystone Center released a report entitled "Improving the Use of Science in Regulatory Decision-Making."[20] This report stressed the importance of consistency and transparency in selecting peer review panels and also noted that the regulatory process is better when there is a consistent, transparent and systematic review and evaluation of the scientific literature.

The importance of a robust peer review process cannot be underestimated. Peer review is essential in the evaluation of scientific information to ensure the development of scientifically defensible assessments. It allows for the review of the underlying assumptions, methodology, criteria, and conclusions reached in the evaluation. Federal Agencies have several mechanisms available to them to conduct peer review of scientific information; however, these peer review processes and approaches are inconsistently applied, including the selection of peer review panel members and the consideration given to public and peer review comments.

For example, during some EPA peer review meetings, the peer reviewers have appeared to be overly deferential to EPA and reluctant to be seen as criticizing EPA staff. We have also seen situations where peer reviewers have suggested discounting a study solely based on the funding source, without any consideration of the quality of the study. Also, EPA staff often comment throughout peer review meetings, essentially participating as peers, while stakeholders, including industry experts, are typically excluded from the

[17] See: http://cdn.bipartisanpolicy.org/wp-content/uploads/sites/default/files/BPC%20Science%20Report%20fnl.pdf.
[18] Ibid, at page 4.
[19] Ibid, at page 45.
[20] See: https://www.keystone.org/wp-content/uploads/2015/08/091812-Research-Integrity-Roundtable-Report.pdf.

dialogue. This practice undermines the integrity of the reviewers' role as independent and external to the assessment itself.

Additionally, a critical element of peer review is the consideration of public comments. The public plays an important role in the review process by helping identify key scientific information and potential concerns with the assessment being evaluated. Unfortunately, within some Agencies, there is no robust consideration of public comments in the peer review process. For example, reviewers on the EPA Science Advisory Board (SAB) are not given clear advice regarding what it means to "consider" public comments. In fact we have seen SAB chairs ignore public input because they are not required to address it. When this has occurred, SAB staff have not clarified to the peer reviewers that they can and should respond to public input.

Improving Systematic Review:

The importance of systematic review in risk evaluation was mentioned in the 2012 Keystone Center report, and emphasized in a 2014 NAS report of its Review of EPA's Integrated Risk Information System (IRIS) Process.[21] This NAS panel noted that the use of systematic review approaches would "substantially strengthen" the IRIS process at EPA. Unfortunately, we have yet to see the IRIS program release an assessment that is consistent with these NAS recommendations.

Data Access and the Protection of Confidential Business Information:

Both the Bipartisan Policy Center report and the Keystone Center report discuss the need to protect proprietary business information. The legitimate need for protection must be balanced against public interest in the disclosure of relevant studies and data for the purposes of reproducibility.[22] The OMB Information Quality Guidelines recognize this tension and note that

> Even in a situation where the original and supporting data are protected by confidentiality concerns, or the analytic computer models or other research methods may be kept confidential to protect intellectual property, it may still be feasible to have the analytic results subject to the reproducibility standard.

When it comes to environmental, health and safety information about chemicals, the Toxic Substances Control Act (TSCA) requires that EPA have access to that information. ACC member companies' current practice is to share summary results of industry studies with EPA or to provide raw data underlying health, safety and environmental studies with EPA upon request. Thus the Agency has the information it needs to ensure the safe regulation of chemicals, and EPA can rely on this information in its regulatory decisions. While any proprietary information must be protected, there are processes that exist to make robust study summary information available to the public in a manner that is sufficient to ensure public understanding of the data and address transparency demands. When it comes to full disclosure to the public, decisions to share raw data with non-regulatory bodies are made on a case by case basis. Companies weigh factors such as the

[21] See: http://dels.nas.edu/Report/Review-Integrated-Risk/18764.
[22] See the Keystone Center report at page 20.

potential health/environmental impact of the product, the commercial value of the data, the age of the data, and other administrative, ethical, financial, legal, technical, and public health considerations.

III. Science Standards in the 2016 Lautenberg Chemical Safety Act

When the Lautenberg Chemical Safety for the 21st Century Act (LCSA)[23] was passed in 2016, it was the first time Congress directed a Federal Agency to consider not only the best available science but also the weight of the scientific evidence (WoE). These scientific standards, added to TSCA in Section 26 of the LCSA, have a prominent role in ensuring the Act achieves the fundamental objective of improving public confidence in the federal regulatory system. EPA now has a mandate to apply high quality, reliable and relevant scientific information.

To date, EPA appears to be interpreting these scientific standards as implying that "business as usual" is consistent with the standards. EPA is reluctant to explicitly incorporate the best available science and WoE standards into the framework rules that it is developing to implement the LCSA. Instead, the Agency has suggested that simple reliance on existing guidelines and current practices are sufficient to meet the standards in Section 26.[24] This is of great concern to ACC.

For example, Section 26(i) of the LCSA requires that EPA make decisions using a WoE approach. While a definition of WoE is not provided in the statute, the June 7 Congressional Record provides a definition that was entered into the record by Senator Boxer, the ranking minority member on the committee:

> Weight of the evidence means a systematic review method that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently, identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance.[25]

This definition is also consistent with the June 2015 House Report language.[26]

Importantly, the definition refers to using a systematic review approach, as has been recommended by the Keystone Center report and the NAS in 2014. It also suggests that evidence be judged on its quality.

Notably, EPA's proposed risk evaluation rule does not incorporate this definition. EPA has asked, however, for comment on this approach.

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[23] P.L. 114-182, 130 Stat. 448 (June 22, 2016).
[24] EPA's draft framework rules for prioritization and risk evaluation can be found at: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/frank-r-lautenberg-chemical-safety-21st-century-act-5.
[25] See Senate Congressional Record, June 7, 2016 at page S3518, available at: https://www.congress.gov/crec/2016/06/07/CREC-2016-06-07-pt1-PgS3511.pdf.
[26] See House Report at page 33, available at: https://www.congress.gov/114/crpt/hrpt176/CRPT-114hrpt176.pdf.

A recent example demonstrates that EPA apparently does not interpret WoE in the same way Congress did in the LCSA. In the draft risk assessment of 1-bromopropane (released prior to enactment of LCSA), EPA did not conduct a systematic review, and the draft assessment did not provide information regarding the quality of the individual studies.[27,28] Although the assessment identified some quality considerations, EPA did not provide any information regarding its own findings from its quality review of the individual studies.[29,30] Additionally, EPA did not describe how considerations were applied and what constitutes a study of "high quality" or "good quality." While EPA staff orally noted that they followed a WoE approach,[31] EPA simply chose the value that provided the lowest point of departure and thus would be most health protective.

The 1-bromopropane draft risk assessment is not consistent with the best available science or the WoE approach envisioned under the LCSA. If EPA chooses to simply follow current practices, the Agency will embark on a process that is not consistent with the new Section 26 science standards.

Section 26 requires EPA to develop, within two years of enactment, any new policies, procedures and guidance that are necessary to ensure compliance with the LCSA. In addition, within five years of enactment and then once every five years, EPA is required to review these policies, procedures and guidance. This approach will ensure that EPA is consistently relying upon scientific approaches that are consistent with the state of the science.

IV. Potential Solutions to Improving Agency Science

ACC provides the following four recommendations to improve the science supporting regulatory decision making.

a. Improve and Clarify Scientific Definitions

ACC believes that the intent of Congress in drafting the scientific standards in the LCSA is clear. It is also clear that EPA's proposed interpretation diverges from Congressional intent in important respects. Clarifying that the intent of scientific standards is to improve existing Agency practices would be useful. In addition, providing clear and specific definitions for terms like best available science and WoE would be beneficial to the consistency, reliability and credibility of EPA's regulatory decisions. These definitions should address not only what Agencies should consider when evaluating scientific information, but also what information

[27] See Comments of the American Chemistry Council on the TSCA Work Plan Chemical Draft Risk Assessment of 1-Bromopropane , Docket No. EPA-HQ-OPPT-2015-0084, May 9, 2016.
[28] See peer review report/meeting minutes available at: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2015-0805-0028, at page 41 which states: "While the Agency indicates that the literature was thoroughly reviewed for robustness, adequacy, etc., the Committee found that it is not clear what exact methodology was used to systematically rate, rank, and select studies to inform sections of the risk assessment. For example, was a quantitative ranking system developed for study quality?"
[29] Ibid.
[30] See draft available at: https://www.epa.gov/sites/production/files/2016-03/documents/1-bp_report_and_appendices_final.pdf, at Appendix M.
[31] See Chemical Safety Advisory Committee Meeting Transcript available at: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2015-0805-0027; at page 130.

Agencies should present in evaluations. Requiring the Agencies to "show their work" and present their thought process in a transparent and clear manner would be have tremendous value. For example, adopting the language from the SDWA Amendments, we suggest the following definition of best available science:

> *Best available science* means information that has been evaluated based on its strengths, limitations and relevance and that the Agency is relying on the highest quality information. In evaluating best available science, the Agency will also consider the peer review of the science, whether the study was conducted in accordance with sound and objective practices, and if the data were collected by accepted methods or best available methods. To ensure transparency regarding best available science the Agency will describe and document any assumptions and methods used, and address variability, uncertainty, the degree of independent verification and peer review.

Defining WoE clearly would also be advantageous. As noted previously, we suggest the definition articulated in the Senate debate on LCSA on June 7, 2016. When using this definition, it will also be important to clearly define the term "systematic review" as there may not be a uniform interpretation of that term among stakeholders.

A particular concern in applying the best available science and weight-of-the-evidence is the tendency of federal agencies to use default assumptions, even when data are available.

Despite more than 30 years of extensive mechanistic toxicological research by academia, research institutions and the private sector, some regulatory programs in EPA continue to rely on default approaches for hazard characterizations and risk assessments that date back to the 1970s. Even though frameworks for integrating mechanistic information and mode of action have been developed by authoritative bodies and incorporated into the EPA cancer risk guidelines,[32] at the present time, there is uneven use within EPA of such approaches in hazard characterizations and risk assessments. EPA's Office of Pesticide Programs has often determined, based on WoE evaluations that include consideration of mode of action and human relevance, that carcinogenic effects in animal studies are not relevant to humans or the carcinogenic effects are secondary to target organ toxicity, and thus no carcinogenic risks are posed to humans at doses below those which produce such toxicities. However, the IRIS program continues to rely on the 1970s default linear approach for cancer risk assessment. The IRIS program steadfast reliance on default linear approaches has significant consequences for many chemicals and can create tremendous costs to address "phantom risks" in site cleanups.[33] This outdated manner in which the EPA IRIS program deals with mode of action knowledge does not comport with use of best available science.

Therefore, in implementing the definitions of best available science and WoE for the evaluation of the potential carcinogenic effects of substances, when supported by the scientific data, EPA should present non-linear modeling approaches consistent with the available data and scientific understanding of endogenous exposures and mode of action, in lieu of, or at a minimum in addition to, a linear default. Further, such assessments should include, in addition to upper

[32] See EPA 2005 Guidelines for Carcinogen Risk Assessment
[33] See George M. Gray and Joshua T. Cohen Nature 489, 27–28, 06 September 2012.

bound calculations, the distribution of estimated hazards or risks, including central tendency values, and clear criteria for when defaults are justified, including criteria for the application of uncertainty factors.

b. Improve Oversight and Develop Quality Checklists

Considering the guidance that already exists from OMB, other consensus bodies, and within the Agencies, stronger oversight to ensure that Agencies are following existing guidance could be highly effective. This oversight could come from independent offices within Agencies, Congress, or OMB or OSTP within the Executive Office of the President. One tool that may be effective is to develop a checklist to ensure that quality standards are met in scientific evaluations that support regulations. For instance, a recent publication from former EPA scientists has suggested that to promote transparency and consistency, risk evaluations could be compared to a guide or checklist which depicts all the important elements of a high quality assessment.[34] Drs. Dellarco and Fenner-Crisp suggest that this guide "could be used by authors, sponsors, risk assessors, peer reviewers, and other interested stakeholders to determine if an assessment meets the current best scientific practices."[35]

c. Improve Peer Review Practices

As noted earlier, the importance of a robust peer review process cannot be underestimated. Ensuring that peer review panels are composed of a diverse group of experts that have the breadth and depth of experience necessary to review scientific analyses in a transparent and comprehensive manner would be beneficial. It is also important to ensure that peer reviewers are fully independent from the program office issuing the assessment and conflicts of interest are fully evaluated and disclosed. More details on improving peer review can be found in the OMB Information Quality Bulletin for Peer Review,[36] as well as in reports from other consensus bodies, as discussed in Section II.

d. Change Publication Incentives and Standards for Scientific Grants and Funding

Much has been written about the lack of reproducibility of research findings published in peer reviewed journals.[37] The trend towards "publish or perish" puts immense pressure on researchers to publish findings, and in particular to publish predominantly positive findings.[38]

Publication bias is common to published academic literature. This leads to bodies of literature in which the majority of publications support a given hypothesis. Publication bias stems from the fact there are many fewer incentives for publishing negative information or information that does

[34] See publication available at: https://ehp.niehs.nih.gov/15-10483/.
[35] Ibid
[36] See: https://www.gpo.gov/fdsys/pkg/FR-2005-01-14/pdf/05-769.pdf.
[37] See for example: http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0020124, or http://www.nature.com/news/reproducibility-1.17552.
[38] See for example: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3999612/.

not support a hypothesis. Promotions and job security in academia, as well as having grants funded by Federal Agencies, are often tied to an author's publication record.

Government Agencies can play an important role by 1) changing the incentives for grant funding such that decisions to fund research do not depend so heavily upon finding positive results and 2) putting in place standards to ensure that research studies are designed in a manner that will make them useable for regulatory decision making. Standards for funding could ensure that research studies follow best scientific practices and are designed with regulatory use in mind. For instance, for chemical risk assessment, studies should be designed to test more than three doses such that a dose-response analysis can be conducted. Unfortunately we have seen too many examples of government funded research where only one high dose is tested. While this information may have some value, it is then difficult to use these data to determine what impact the same chemical may have at more environmentally relevant lower dose ranges. If the government demanded a more robust study design when approving the research projects, the data obtained would likely be much more useful.

V. Conclusion

Ensuring that Federal decision making is firmly based on the use of high quality science is critical to helping the government meet its obligation to protect human health and the environment. This can be achieved through common sense reforms that will lead to more efficient and effective regulatory decisions. ACC looks forward to working with members of the Committee to enhance approaches to ensure that high quality science is the foundation to regulatory decision making.

Appendix 1: Examples of Scientific Concerns with Federal Science Evaluations

Below ACC provides a few specific examples where Federal Agencies have fallen short when it comes to using the best available science.

a. Case 1: OSHA Crystalline Silica PEL

Background
OSHA finalized its workplace Permissible Exposure Limit (PEL) for crystalline silica in March, 2016. The final PEL reduced the standard from 100 $\mu g/m^3$ to 50 $\mu g/m^3$.

Crystalline silica (commonly encountered as beach sand) is the second most abundant mineral in the Earth's crust. It is ubiquitous in rocks, gravel, sand and soils; plays a crucial role in construction and transportation; and is essential for many manufacturing processes and countless products. For example, it is a critical material for foundries and steel making, and is a key component of abrasives, paints, high-tech equipment, glass and ceramics.

OSHA contended that the PEL of 100 $\mu g/m^3$ was not sufficiently protective. In fact, however, the data clearly shows that the incidence and rate of silicosis mortality have declined dramatically since adoption of the 100 $\mu g/m^3$ PEL in 1971, and the remaining cases can be attributed to higher silica exposures that were prevalent decades ago (allowing for latency) and to exceedances of the 100 $\mu g/m^3$ PEL. Moreover, the best evidence indicates that for silicosis and other potential pulmonary diseases, including lung cancer, there is a concentration-based threshold for silica exposure that exceeds 100 $\mu g/m^3$.

Importance
The new PEL is not economically feasible across multiple sectors of general industry and therefore will cause significant economic disruption throughout the economy. OSHA estimated that the annualized costs for all of general industry to comply with the revised standard would be $359 million. That estimate of compliance costs is deeply flawed and vastly understates the true costs of compliance, which are likely to be more than an order of magnitude higher. It would be far more cost-efficient and effective to bring all general industry employers into compliance with the longstanding PEL of 100 $\mu g/m^3$ rather than mandating that they attempt to comply with the new PEL of 50 $\mu g/m^3$.

Scientific Concerns
Because of its long latency period, silicosis cases seen today are attributable largely to exposures that occurred decades ago – in most cases, to exposures that began before OSHA's long-standing PEL of 100 $\mu g/m^3$ was even adopted. OSHA's argument that silicosis cases are underreported does not alter the fact that silicosis cases have dropped dramatically in the previous 40+ years, as silicosis cases have been underreported relatively consistently through that same time period. There are fundamental shortcomings and limitations in OSHA's risk assessment for all of OSHA's identified endpoints of concern:

- Important statistical errors in modeling and inference, including in particular a failure to adequately control for biases, which can lead to false positive results.

- A failure to properly model exposure measurement errors, which are common in the silica worker cohort studies in particular.
- Generally, uncertainties are not well characterized in the preliminary quantitative risk assessment.
- A failure by OSHA to carry out any causal modeling or analysis that would allow it to conclude that a reduction in the PEL would actually reduce adverse health effects.

The alleged association between silica exposure *per se* and lung cancer remains controversial in the scientific community. OSHA did not properly weigh and consider the totality of the epidemiological evidence, discounting the significance of negative studies while choosing to highlight those studies that would confirm OSHA's position. Furthermore, as noted above, the best evidence points to an exposure concentration threshold for potential silica-related lung cancer that exceeds the PEL of 100 $\mu g/m^3$ that applied in general industry before the new rule was adopted in 2016.

b. Case 2: EPA IRIS Assessment of Trimethylbenzenes (TMB)

Background
On September 9, 2016, EPA issued its final report on the IRIS assessment of Trimethylbenzenes (TMBs), which addresses the potential non-cancer and cancer human health effects from long-term exposure to TMBs. Humans are not exposed to individual TMB compounds, but to complex mixtures. According to EPA, the primary uses for TMBs are as a blending agent in gasoline formulations (C9 aromatic fraction); solvents; and as a paint thinner.

In its review of TMBs, the EPA fell far short in meeting its obligations to improve its IRIS processes and assessment reports. Without explanation, EPA failed to respond to public comments on the draft TMBs assessment, even though the IRIS process for developing assessments explicitly includes a response to comments element.

Importance
As a final report, the IRIS assessment on TMBs will inform risk management decisions on TMBs by EPA's program and regional offices.

Scientific Concerns
The IRIS assessment of TMBs does not accurately represent the health effects associated with exposure to TMBs because EPA failed to utilize a consistent and transparent data evaluation procedure for evaluating and weighing the full body of evidence.

In particular, EPA failed to rely on available guideline studies on commercial complex C9 aromatic mixtures that industry conducted under EPA's TSCA program. The entire commercial C9 aromatic blend, which contains a high percentage of TMBs, has similar toxicological properties and health effects as the individual isomers of TMB. Thus, guideline studies on the commercial complex of aromatic mixtures are highly relevant to assessing the toxicology of TMBs.

EPA's Office of Pesticide Programs (OPP) has also reviewed the toxicology of TMBs and determined that the health effects of TMBs can be efficiently assessed by relying on C9 aromatic

mixture studies. OPP reached different scientific conclusions, including different quantitative health effect numbers, than that of EPA's IRIS Program. EPA, however, did not resolve these differences during the IRIS assessment of TMBs.

c. Case 3: NIOSH Cancer Policy

Background

In the NIOSH Carcinogen Policy, released in December 2016, NIOSH states that underlying this entire policy is the "recognition that there is no known safe level of exposure to a carcinogen."[39] ACC believes this statement is based on a default assumption and not clear scientific evidence, as certain carcinogens have thresholds or doses below which no adverse effects are identified.[40,41] Assuming that every chemical is toxic at high exposures and linear at low exposures does not comport with modern-day scientific knowledge of biology and there is no compelling evidence-based justification for a general low-exposure linearity. Instead, case-specific mechanistic arguments are needed.[42]

d. Case 4: EPA IRIS Assessment of Ethylene Oxide (EO)

Background

EPA posted the final IRIS Assessment of EO in December 2016. EPA, using unsupportable, conservative, risk assessment modeling, concluded that the one-in-a-million lifetime cancer risk associated with exposure to EO is far below EO background levels currently in the environment and EO levels naturally converted from ethylene in humans through breathing.

This conclusion is not plausible, and not scientifically supportable. It is based on an inadequate evaluation of a body of evidence from human studies that include historical exposure levels to

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[39] See NIOSH Carcinogen Policy available at: https://www.cdc.gov/niosh/docs/2017-100/default.html.

[40] See, for example Olden K, Vulimiri SV. 2014. Laboratory to community: chemoprevention is the answer. Cancer Prev Res (Phila). 7(7):648-52. http://cancerpreventionresearch.aacrjournals.org/content/canprevres/7/7/648.full.pdf at 650; which states: "Our understanding of toxicologic mechanisms has advanced considerably since the linear non-threshold model was adapted for cancer risk assessment. Knowledge of mechanism of action is critical for informing dose–response relationship below the experimental observable range. Johnson and colleagues (1) have used new technologies in analytical chemistry and molecular biology to characterize downstream biologic events in the exposure disease continuum. They showed that AFB1 is a classic genotoxic substance in that it binds covalently to DNA and induces mutations. In fact, DNA adduct formation exhibits a characteristic linear dose–response curve over a wide range. But, further analysis demonstrated a threshold mode of action, with respect to internal dose of active metabolite and hepatocarcinogenesis. That is, there was substantial adduct formation and DNA damage without having any affect [sic] on development of hepatocellular carcinoma."

[41] See, for example: United States Environmental Protection Agency (EPA). 2015. Chemicals evaluated for carcinogenic potential office of pesticide programs, annual cancer report. Washington, DC. http://npic.orst.edu/chemicals_evaluated.pdf. EPA has determined that a number of substances that produce cancer at high doses are not likely to be carcinogenic to humans at low doses.

[42] Rhomberg LR, Goodman JE, Haber LT, Dourson M, Andersen ME, Klaunig JE, Meek B, Price PS, McClellan RO, Cohen SM. 2011. Linear low-dose extrapolation for noncancer health effects is the exception, not the rule. Crit Rev Toxicol. 41(1):1-19. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3038594/pdf/btxc12-001.pdf and Bogen, KT. 2016. Linear-No-Threshold Default Assumptions for Noncancer and Nongenotoxic Cancer Risks: A Mathematical and Biological Critique. Risk Analysis Risk Analysis, Vol. 36, No. 3. http://onlinelibrary.wiley.com/doi/10.1111/risa.12460/pdf. .

EO that are far higher than current occupational exposure limits. Other, more accurate, data sources are available, and alternative scientific risk assessment modeling approaches could have been used, but EPA made no serious, systematic attempt to integrate all of the evidence.

Importance

A determination by EPA that EO, with a myriad of important applications including the sterilization of medical equipment for surgery, can cause cancer at less than one part-per-trillion[43] exposure will needlessly cause alarm and confusion, not only among workers, but also in the general population and in the public health and medical communities. These numbers are not reliably measurable, and are orders of magnitude below current endogenous and exogenous levels of EO.

Scientific Concerns

EPA did not adequately consider study quality into the IRIS review. Industry cohorts were not considered with the other epidemiology data sets even though this cohort was stronger than foreign cohorts used that contained occupational exposure interferences.

EPA did not fully utilize linear and non-linear modeling approaches (as allowed within the cancer assessment guidance) to estimate cancer risk from current EO exposure levels and expected DNA repair mechanisms.

EPA did not consider realistic exposure scenarios and fully delineate endogenous vs. exogenous EO and associated health impacts.

In 2007, EPA's SAB identified problems with the linear regression modeling and low dose extrapolation for determining cancer risk. The SAB concluded that substantial revisions were needed in the IRIS assessment including:

- Acquiring and using individual data for modeling rather than grouping populations for modeling that currently results in overly conservative estimated cancer risks;
- Given the distribution of and questionable association with certain cancer types, considering using both linear and non-linear approaches to estimate cancer risk;
- Providing more transparency and correcting flaws associated with inappropriately grouping lymphohematopoietic (LH) cancers and combining genders for the dose-response analysis.

In 2015, a specially selected SAB Committee reviewed a revised draft EO IRIS assessment. The committee, however, did not conduct an independent, unbiased review. Problems included:

- Inaccurate public statements by several SAB members indicating industry produced scientific studies should be disqualified due to potential industry influence, and the acceptance by SAB and IRIS staff of such a position; no evidence of biased data sponsored by industry was ever presented, and it is clear that those members advocating this position should have been disqualified due to these clear biased positions.

[43] 1 part per trillion is roughly equivalent to 1 second in 320 centuries or 1 inch in 16,000,000 miles

- Lack of understanding by SAB members of new evidence-based medicine concepts regarding mutagenicity of cancer cells and the contribution of naturally occurring EO in DNA repair mechanisms;
- Recommendation of epidemiology data sets with questionable or scientifically unsound characteristics to estimate cancer risk and rejection of alternative data sets that are as or more robust than those selected;
- EPA still did not use individual data for modeling as recommended in 2007, and did not seriously explore alternatives to the linear low dose modeling approach.

Even though the SAB made extensive recommendations in its 2015 report and public comments were submitted on the IRIS draft reviewed by the SAB, EPA still did not respond fully to all comments submitted or implement all the changes recommended by the SAB.

e. Case 5: National Ambient Air Quality Standard for Ground-Level Ozone

Background

In 2015, EPA lowered the National Ambient Air Quality Standard (NAAQS) for Ground-Level Ozone from 75 ppb to 70 ppb. Ozone, which is one of six criteria pollutants regulated under Section 109 of the Clean Air Act, is formed from a reaction between nitrogen oxide (NOx), volatile organic compounds (VOCs), and sunlight. Exposure to relatively high concentrations of ozone can cause adverse respiratory effects and interfere with plants' ability to produce and store food.

In 2008, the ozone NAAQS was set at 75 ppb. Areas were not designated as complying or failing to comply with this standard until May 2012 due to unnecessary delays following the Obama Administration's premature reconsideration of the standard in 2010. This resulted in areas across the country not being allowed sufficient time to begin implementing the 2008 standard before EPA changed the standard again, which the Agency justified as being necessary to protect public health and welfare. However, a closer look at EPA's work during this most recent review process questions the need to revise down the standard.

Scientific Concerns

EPA relied on ecological epidemiology studies, also known as time-series analyses and clinical studies, as the basis to lower the ozone NAAQS to 70 ppb in 2015. However, EPA failed to adequately characterize the uncertainties associated with adverse health effects reported in these studies. Ecological epidemiology studies are not scientifically rigorous enough and are not designed to determine if ozone was responsible for the demonstrated the health effects. Clinical studies are limited by the small sample sizes and because they do not adequately consider the normal variation in the lung function.

For example, in the 2015 standard, EPA relied on two new studies, Schelegle *et al.* (2009)[44] and Kim *et al.* (2011).[45] These studies both used a small sample which, while not unusual for a

[44] Schelegle, ES; Morales, CA; Walby, WF; Marion, S; Allen, RP. 2009. 6.6-Hour inhalation of ozone concentrations from 60 to 87 parts per billion in healthy humans. Am. J. Respir. Crit. Care Med. 180(3):265-272.
[45] Kim, CS; Alexis, NE; Rappold, AG; Kehrl, H; Hazucha, MJ; Lay, JC; Schmitt, MT; Case, M; Devlin, RB; Peden, DB; Diaz-Sanchez, D. 2011. Lung function and inflammatory responses in healthy young adults exposed to 0.06 ppm ozone for 6.6 hours. Am. J. Respir. Crit. Care Med. 183:1215-1221.

controlled human exposure study, proves difficult as a basis for drawing broader conclusions with regard to the protection of public health. EPA identified lung function decrements of only 2.8% to be adverse effects when the variation of lung function in normal subjects can vary by over 5% (Pellegrino *et al*. 2005)[46] to 17.6% (Medarov *et al*. 2008).[47] EPA must rely on biological, not just statistical, significance in identifying an adverse health and provide clear guidance on how to define adverse effects.

Ultimately, these studies did not actually support health effects below the 75 ppb standard, and EPA primarily justified the regulation impacting 300 million people on study results from just a few individuals.

[46] Pelligrino, R; Viegi, G; Brusasco, V; Crapo, RO; Burgos, F; Casaburi, R; Coates, A; van der Grinten, CPM; Gustafsson, P; Hankinson, J; Jensen, R; Johnson, DC; MacIntyre, N; McKay, R; Miller, MR; Navajas, D; Pedersen, OF; Wanger, J. 2005. Interpretive strategies for lung function tests. Eur. Respir J. 26: 948-968.
[47] Medarov BI, Pavlov VA, Rossoff L. 2008. Diurnal variations in human pulmonary function. Int J Clin Exp Med. 1(3):267-273.