August 16, 2018

Dr. Thomas Sinks
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Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, DC 20460-0001

Submitted electronically to www.regulations.gov

Re: EPA Docket EPA-HQ-OA-2018-0259;
Comments of the American Chemistry Council on EPA's Strengthening Transparency in Regulatory Science Proposed Rule

Dear Dr. Sinks:

The American Chemistry Council is pleased to submit the attached comments on the Environmental Protection Agency's proposed rule, Strengthening Transparency in Regulatory Science.

Please contact me should you have any questions regarding these comments at 202-249-6406 or Christina_Franz@americanchemistry.com.

Sincerely,

Christina Franz

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Senior Director, Regulatory & Technical Affairs
American Chemistry Council

Comments of the American Chemistry Council on EPA's Strengthening Transparency in Regulatory Science Proposed Rule

EPA Docket EPA-HQ-OA-2018-0259

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Executive Summary

The American Chemistry Council (ACC) is pleased to provide the following comments on the Environmental Protection Agency's (EPA) proposed rule, Strengthening Transparency in Regulatory Science (Strengthening Transparency), published in the Federal Register on April 30, 2018.[1] ACC and its members are directly impacted by the science-based regulatory actions of EPA under a myriad of federal environmental statutes. As such, ACC has a keen interest in EPA's adoption and implementation of a proposal as important as this one, which will reach across the breadth of the Agency's authority.

In the following comments, ACC offers its support for the proposed rule; responds to a number of questions posed by EPA in its preamble; and provides a number of specific recommendations regarding how the proposed rule can be improved and strengthened. Specifically, ACC suggests the following:

- Implementation of the rule would benefit from policy and/or guidance regarding the weight to be accorded the science informing significant regulatory decisions
- EPA should provide better historical context and applicability to the proposed rule
- EPA has not in all circumstances properly identified from where its authority is derived under the various federal environmental statutes cited in the proposed rule
- The regulation should apply to Executive Order 12866 significant regulatory actions at the proposal stage
- Key regulatory definitions and regulatory text require greater clarity
- Clarifications to the preamble are needed
- Implementation of the rule should be statute specific
- The proposed rule should apply to enforcement and permit proceedings
- EPA should incorporate stronger data and model access requirements into its Cooperative Agreements and Grants while complying with privacy and confidentiality requirements and laws
- The rule should apply to all EPA programs, including its IRIS program
- Methodologies and technologies providing protected access to confidential and sensitive data should be employed

[1] 83 FR 18768 (April 30, 2018).

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- The rule should generally apply prospectively to EPA decision making
- Bias should not be presumed
- EPA should work with entities where scientific data are not publicly available in a manner sufficient for independent evaluation

I. Introduction and Background

ACC strongly supports EPA's demonstrated commitment in this proposal to build upon the principles underlying the Administrative Procedure Act (APA), Executive Orders 12866, 13777, and 13783, and guidance of Office of Management and Budget (OMB). In addition, ACC supports the proposal's expansion of the 2013 "Increasing Access to the Results of Federally Funded Scientific Research" memorandum directing federal agencies and offices to develop and submit plans to the White House Office of Science and Technology (OSTP) that ensure peer-reviewed publications and digital scientific data resulting from federally-funded scientific research are accessible to the public, the scientific community, and industry—to the extent practicable.

The OSTP directive required each agency to develop a public access plan that maximizes access to federally-funded "digitally formatted scientific data"[2] while also protecting confidentiality, personal privacy, confidential business information (CBI), intellectual property rights, and U.S. competitiveness.[3] In 2016, EPA issued its Plan to Increase Access to Results of EPA-funded Scientific Research in response to the OSTP directive.[4] Importantly, EPA's Strengthening Transparency proposal appears to extend such commitments beyond the government-funded requirement of the OSTP directive to "dose response data and models underlying pivotal regulatory science regardless of the source of funding or identity of the party conducting the regulatory science."[5]

ACC believes that EPA's proposal correctly codifies an important good governance principle—that government agencies should be as transparent as possible, within the bounds of the law, about scientific information relied upon and the justifications for the significant regulatory decisions they make.

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[2] As defined in OMB circular 110 as "the digital recorded factual material commonly accepted in the scientific community as necessary to validate research findings, including data sets used to support scholarly publications. . ." It is a definition consistent with that of "research data" in the regulatory text of EPA's proposal.

[3] More than 20 federal agencies have developed and implemented Data Access Plans, including EPA, the National Institutes of Health (NIH), the Center for Disease Control (CDC), and the Food and Drug Administration (FDA).

[4] Plan to Increase Access to Results of EPA-Funded Scientific Research (USEPA, November 29, 2016) https://www.epa.gov/sites/production/files/2016-12/documents/epascientificresearchtransperancyplan.pdf

[5] ACC suggests improvements to EPA's terminology in the preamble that are described later in these comments in sections VI and VII.

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The Agency's focus on dose-response data and models appropriately reflects the evolution of toxicology from a largely observational science to a discipline that applies advanced scientific techniques and knowledge. Research programs within academia, government, and private sector labs have greatly improved our ability to investigate and understand the underlying biological mechanisms, modes of action, and dose responses of toxicants. We can now evaluate biological events leading to toxicity and consider how (in a dose-response manner) these biological events relate to potential risks to human health. This was not possible 10-to-20 years ago. This improvement should directly translate to the application of transparent weight-of-the-evidence approaches to the assessment of human relevance; the development of points of departure; and the derivation of protective human health equivalent dosages that minimize the use of uncertainty factors and variability. A goal has been to apply this knowledge to improve the scientific basis of government regulatory policies and industry product stewardship.

For environmental concerns, exposure-response is the more appropriate relationship to evaluate because most of the environmental test guidelines require quantifying concentrations in media external to the organism for use as the exposure metric. Toxicity information and—when available—knowledge of mechanisms, are integrated with exposure-response models for risk-based environmental safety decision making.

Despite significant scientific progress in the understanding of mechanisms of action (MOA) and adverse outcome pathways (AOP), the movement away from default precautionary assumptions has been slow to occur, particularly in certain EPA programs. Significant investments by government, academia, and the private sector into toxicological research are counteracted by the failure to move away from default assumptions toward science-based decisions.

ACC encourages EPA to implement best available scientific procedures under this rulemaking. The Agency should move away from the outdated linear concept of how biology operates toward biologically-based mechanisms, i.e., mode of action (MOA) and adverse outcome pathways (AOP) for both cancer and non-cancer effects, that clearly establish the threshold nature of toxicological endpoints for derivation of points of departure for establishing regulatory values and making regulatory decisions.[6] [7]

In the following discussion, ACC offers its comments to help clarify and strengthen the proposed rule.

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[6] Critics of this proposed policy appear to overlook the fact that the call to evaluate different dose response models is entirely consistent with the Agency's Cancer Guidelines, which have been in place since 2005. See Guidelines for Carcinogen Risk Assessment https://www.epa.gov/sites/production/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf

[7] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3038594/

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II. Implementation of the Rule Would Benefit from Policy and/or Guidance Regarding Weight Accorded the Science Informing Significant Regulatory Decisions

As EPA has noted, the proposed rule is consistent with and builds upon the EPA policies implemented by previous administrations. Implementation would be aided by a policy statement or guidance that indicates greater weight will be given to studies using validated test methods and procedures, models, and approaches when and where those data are based on publicly accessible data, and transparent computer algorithms.

Other scientifically relevant and reliable studies and data should not be eliminated from consideration, but rather, accorded less weight when integrating evidence from multiple studies within and across different lines of evidence. Any guidance and other relevant documents developed to assist EPA staff to comply with this rule should include specific examples and/or case studies, perhaps drawing from recent EPA rulemakings, to demonstrate what constitutes regulatory science that is material to EPA's significant regulatory decisions.

III. EPA Should Provide Better Historical Context and Applicability to the Proposed Rule

EPA is proposing to add this rule to 40 C.F.R. 30, contained in Chapter 1, Subchapter B, dedicated to "Grants and Other Federal Assistance," without explaining how or why this rule fits within this subchapter, thereby creating potential confusion regarding its applicability. The potential for confusion was enhanced by the fact that EPA's public website currently contains information regarding the content that was formerly within 40 C.F.R. 30 but was repealed on December 19, 2014, i.e., general terms and conditions applicable to grant recipient and sub-recipients.[8] In addition, a number of questions on which EPA seeks comment relate solely to EPA cooperative agreements and grants or access to EPA-funded data.

In contrast, Section 30.3 of the proposed regulatory text state that "the provisions of this section apply to dose-response data and models underlying pivotal regulatory science regardless of who funded or conducted the underlying data, models, or other regulatory science." Stakeholders would benefit greatly from EPA providing clarification regarding the applicability of Subchapter B and whether and to what extent this rule applies to government-funded and/or beyond government-funded scientific research. We believe the broader approach is warranted.

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[8] https://www.epa.gov/grants/epa-general-terms-and-conditions-applicable-40-cfr-part-30-and-31-recipients-effective and see, 79 Fed. Reg. 244 at 76054 (Dec. 19, 2014).

IV. EPA Authority under Federal Environmental Statutes

The provisions cited by EPA under the Clean Air Act (CAA), the Clean Water Act (CWA), the Safe Drinking Water Act (SDWA), the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), and the Emergency Planning and Community Right-To-Know Act (EPCRA) in support of its authority to develop and implement its proposed rule all provide broad regulatory authority to promulgate regulations "as are necessary to carry out [the Administrator's] functions" under the statute. The citation to the Resource Conservation and Recovery Act (RCRA) speaks to Labor Standards in the issuance of grants, and does not appear applicable to this rulemaking authority. EPA cites Section 25(a)(1) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), which does provide the Agency with broad authority to "prescribe regulations to carry out the provisions of this subchapter [FIFRA]." It should be noted, however, that the statutory language is a bit different from the other cited statutes and does not read as "as are necessary to carry out….". In addition, FIFRA Section 136r(a) does not relate to rulemaking and instead provides the Agency broad authority to undertake research necessary to carry out the purposes of FIFRA. As such, EPA may mistakenly have included Section 136r(a) to support the proposal as cited on 83 Fed. Reg. 18769. EPA's reference to section 10 under the Toxic Substances Control Act (TSCA) also does not appear on-point. ACC believes EPA's authority to implement this rule is derived from TSCA Section 26(h), which speaks directly to scientific information and standards to which the Agency must adhere in the administration of its work under TSCA Sections 4, 5, and 6.

V. The Regulation Should Apply to E.O. 12866 Significant Regulatory Actions at the Proposal Stage

A. <u>Definitions in E.O. 12866 Are Well-Established, Understood, and Applied</u>.

The proposed rule would apply to significant regulatory actions as defined by E.O. 12866 at Section 3(f) as:

> (f) ''Significant regulatory action'' means any regulatory action that is likely to result in a rule that may:
>
> > (1) Have an annual effect on the economy of $100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities;
> > (2) Create a serious inconsistency or otherwise interfere with an action taken or planned by another agency;
> > (3) Materially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or
> > (4) Raise novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in this Executive order.

This definition has been applied by the Executive Branch since the Clinton Administration promulgated E.O. 12866 in 1993. Its meaning is well-established with more than twenty-

five years of use. The underlying principles, however, precede its adoption. For example, the E.O. carried over the threshold of an annual $100 million effect on the economy that had been in place since 1978. This (3)(f)(1) threshold for economically significant regulatory actions is the same threshold that requires cost-benefit review for proposed and final regulations considered by OIRA.

A significant benefit of using the E.O. 12866 definition in the final rule is that EPA can easily apply it, against substantial practice and precedent, in a reliable, consistent, and predictable manner. This reduces the burden on the agency, and importantly, provides greater predictability to stakeholders and the public so they can understand to which agency actions the regulation will apply.

B. Conformity with E.O. 12866 Definitions Promotes Efficient OIRA Review.

Similarly, the process by which significant regulatory actions are identified under E.O. 12866 is also well-established. Here, with respect to application of the proposed rule, EPA would retain primary responsibility to identify the significant regulatory actions to which the rule should apply. OIRA would assess EPA's identification against the criteria set out in E.O. 12866. Neither EPA nor OIRA would be charged with applying a new or unfamiliar definition, nor a new process for review.

C. The Range of Agency Actions to Which the Rule Will Apply Should Not be Narrowed.

The significant regulatory elements of E.O. 12866 already require OIRA review and have for the past 25 years of established practice. The proposed rule respects that principle, and indeed, leverages it for maximum efficiency.

EPA specifically invites comment on whether a narrower definition might be appropriate, such as final regulations that are determined to be "major" under the Congressional Review Act, or "economically significant" under E.O. 12866. Either of these approaches would lose the efficiency and predictability benefits of using the E.O. 12866 definition—and would increase work for both EPA and OIRA. Further, many significant and precedential agency actions do not meet the "economically significant" threshold. For example, many federal agencies administer environmental, health and safety requirements for workers, consumer products, and environmental media—air, water, soil. It should never be the case that EPA, or EPA and other agencies, establish and/or enforce conflicting and irreconcilable health values for the same compound; require the use of different personal protective equipment; or simultaneously prohibit and permit use or discharge of a particular compound. The same rigorous scientific standards, best available science and weight-of-the-evidence approaches should be applied across programs and media to protect human health and the environment. Adoption of the E.O. 12866 definition of significant regulatory action helps avoid inconsistent regulatory decisions by federal agencies that might interfere with policies designed to protect human health and the environment, unfairly burden businesses, and impede the protection of human health and the environment.

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D. The Final Rule Should Apply to Significant Guidance Documents.

OMB's Final Bulletin for Agency Good Guidance Practices defines a "significant guidance document" as a guidance document disseminated to regulated entities or the general public that may reasonably be anticipated to:

> (i) Lead to an annual effect on the economy of $100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or state, local, or tribal governments or communities;
> (ii) Create a serious inconsistency or otherwise interfere with an action taken or planned by another agency;
> (iii) Materially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or
> (iv) Raise novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in EO 12866, as further amended.

EPA already maintains and publishes a list of significant guidance documents that meet the OMB definition.[9] [10] Applying the rule to EPA's significant guidance allows for greater parity and consistency with respect to the application of scientific principles in regulatory and guidance contexts. It ensures that the same quality and rigor will underpin decision making. It also helps ensure that EPA will apply the same principles to both regulatory requirements and implementing guidance, which provides greater certainty to the regulated community and the public.

VI. Key Regulatory Definitions and Regulatory Text Require Greater Clarity

EPA's terminology and regulatory definitions should be more concise and applied consistently to achieve greater clarity regarding the meaning and proposed application of the rule. For example, proposed section 30.2 refers to "**pivotal** regulatory science as the studies or analyses that **drive** the requirements and/or quantitative analysis of EPA final significant regulatory decisions." [Emphasis added]. This definition is distinguished from "regulatory science," defined as "scientific information, including assessments, models, criteria documents, and regulatory impact analyses, that provide the basis for EPA final significant regulatory decisions." These two definitions can be interpreted as simultaneously referencing something identical as well as one being a subset of the other. Therefore, the definitions are vague and need clarification.

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[9] See https://www.epa.gov/laws-regulations/significant-guidance-documents

[10] Notably, EPA's list of significant guidance documents include guidance that applies directly to the regulated community, such as the agency's *2017 Guidance To Assist Interested Persons in Developing and Submitting Draft Risk Evaluations Under the Toxic Substances Control Act* (EPA-HQ-OPPT-2017-0341-0002) and *Interpretive Guidance for the Real Estate Community on the Requirements for Disclosure of Information Concerning Lead-Based Paint in Housing, Part I* (EPA-HQ-OPPT-2007-0765-0001).

Assuming the intent is to define and distinguish the subset of scientific studies and analyses that form the scientific foundation for EPA's regulatory decisions from the larger universe of *all* the scientific information reviewed and considered by the agency, a more precise word than "pivotal" would be "material." In other words, those scientific studies and analyses that are material to its regulatory decision must be or be made publicly available in a manner sufficient for independent validation.

The regulatory text in 30.4 and 30.5 should be clarified. Section 30.4 appears to apply to EPA's use of studies (or other regulatory science) relied upon when EPA takes *any* final agency action (emphasis added). In those instances, EPA should make all such studies available to the public to the "extent practicable." Section 30.5 refers specifically to the requirements that apply when "EPA uses dose response data and models underlying "pivotal" (which ACC believes is more aptly expressed as "material") regulatory science." ACC interprets this to mean that in these specific circumstances, the dose response data and models must be "publicly available in a manner sufficient for independent validation," which EPA defines as in a manner "consistent with law, protects privacy, confidentiality, confidential business information, and is sensitive to national and homeland security." Information considered "publicly available in a manner sufficient for independent validation" when it includes the information "necessary for the public to understand, assess, and replicate findings." As noted above, for environmental safety, exposure-response is the more appropriate relationship to evaluate because most of the environmental test guidelines require quantifying concentrations in media external to the organism for use as the exposure metric. EPA should provide greater clarity regarding what it intends to do in circumstances where raw data cannot be made publicly available.

EPA should include a discussion in the final rule regarding how it proposes to address exposure assessments and risk characterization data and models in the future extensions of related rules on Transparency in Regulatory Science.

Section 30.7 appears to be missing one or more words in the header to the section. It states: "What role does independent peer review in this section?" ACC believes the missing word is likely "have," but EPA should clarify and correct this section in the final rule.

EPA uses the word "justify" frequently throughout the various sections of proposed regulatory text when referencing the use of regulatory science to make its decisions. For example, section 30.7 states: "EPA shall conduct independent peer review on all *pivotal regulatory science* used to justify *regulatory decisions.*" ACC suggests that there are more precise words that EPA should use to link "pivotal regulatory science" with "regulatory decisions," such as "underpin" or constitute the "foundation" of the "scientific basis" of its regulatory decisions.

ACC has offered some additional, specific language suggestions in a redline version of the proposed regulatory text that is included in these comments in Appendix A.

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VII. Clarifications to the Preamble are Needed

A. Definition of "Pivotal Regulatory Science" is needed.

The definition in the proposed regulatory text and may lead to confusion among stakeholders. We recommend consistency between the preamble and the regulatory text and that EPA clarify its terminology.

Importantly, in footnote three on page 18769 of the preamble, EPA states:

> EPA has the authority to establish policies governing its reliance on science in the administration of its regulatory functions. Historically, EPA has not consistently observed the policies underlying this proposal, and courts have at times upheld EPA's use [of] non-public data in support of its regulatory actions. *See Coalition of Battery Recyclers Ass'n v. EPA,* 604 F.3d 613, 623 (D.C. Cir. 2010); *American Trucking Ass'n v. EPA,* 283 F.3d 355, 372 (D.C. Cir.2002). EPA is proposing to exercise its discretionary authority to establish a policy that would preclude it from using such data in future regulatory actions.

ACC believes that this footnote should be clarified to be consistent with the regulatory text that provides that there are exemptions to this policy outlined in sections 30.5 and 30.9. EPA's preamble should not be at odds with the regulatory text.

Invariably there will be circumstances where underlying data no longer exist for studies and/or models that are high quality and reliable. For example, most organizations have data retention policies that have resulted in the disposal of underlying data. Furthermore, Good Laboratory Practices (GLP) regulations include defined periods of time to retain data and study records.[11] EPA should address how it will continue to use those studies and models in light of these policies.

B. Assertions about proposal not "directly regulating entities outside of federal government" and not having "substantial direct effects" on the states.

On page 18769 under section A, EPA states that the proposed regulation does not "directly regulate any entity outside the federal government" and on page 18772, EPA states under section E that "this action imposes no enforceable duty on any state, local or tribal governments or the private sector." Under Section F, EPA asserts that this action does not have federalism implications and will not have "substantial direct effects on the states." ACC is not certain that these statements are accurate. Consider, for example, the establishment of water quality standards (WQS).

[11] 40 C.F.R. 160.

Under Section 303(c) of the CWA, states and authorized tribes must develop WQS and submit them to EPA for its approval or disapproval. To help them develop the standards, EPA provides scientific guidance through its "Section 304(a) National Criteria Recommendations," which specify quantitative concentrations/level and qualitative measures of pollutants that, if not exceeded, generally will ensure acceptable water quality. In developing these recommendations, EPA evaluates acceptable water quality. When developing these recommendations, EPA evaluates available scientific data on a pollutant's effects on public health and welfare, aquatic life, and recreation. EPA recommends that states and tribes consider the Agency's water quality criteria when developing their WQS, though states and tribes may also consider other scientific criteria that differ from EPA's recommendations.

While EPA's national water quality criteria recommendations are not regulations and do not impose binding requirements, they do serve as the scientific basis for the development of water quality standards and WQS are the foundation of a number of CWA programs. As EPA states in its Water Quality Standards Handbook, these standards "establish the baseline used for measuring the success of the CWA programs, so adequate protection of aquatic life and wildlife, recreational uses, and sources of drinking water, for example, depends on developing and adopting well-crafted WQS."[12]

C. Publications should be cited.

ACC suggests that EPA revise its statement that the proposed rule "takes into consideration the policies or recommendations of third-party organizations who [sic] advocated for open science." The recommendations referenced by EPA actually emanate from a survey of the members of three professional organizations whose memberships represent repositories of knowledge and experience in regulatory assessment.[13] As such, reference 10 in EPA's proposal should also be revised to cite the publication, Expert Opinion on Regulatory Risk Assessment, A Survey by the Center for Media and Public Affairs (CMPA) and Center for Health and Risk Communication (CHRC) at George Mason University" (December 6, 2013).[14]

D. Definition of "reproducibility" is needed.

EPA uses the term "reproducibility" in the preamble, but never defines the term and does not include the term in the definitions in the proposed regulatory text. It is unclear what constitutes a reproducible versus non-reproducible finding. It is important to consider that there are different types of reproducibility, such as methods reproducibility, results reproducibility, and reproducibility of conclusions.

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[12] Water Quality Standards Handbook, Office of Water, EPA 820-B-14-008, September 2014, at p. 2.
[13] The Risk Assessment Specialty Section of the Society of Toxicology (SOT-RASS), the Dose Response Section of the Society for Risk Analysis (SRADRS), and the International Society for Regulatory Toxicology and Pharmacology (ISTRP).
[14] https://cmpa.gmu.edu/wp-content/uploads/2013/12/GMU-Study-Report.pdf.

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For example, OMB's Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies defines "capable of being substantially reproduced" as "independent reanalysis of the original or supporting data using the same methods would generate similar analytical results, subject to an acceptable degree of imprecision." [15] However, the inability to reproduce research studies can be related to issues of study design, variability or differences in biological test systems, data integrity, data analyses, and in some cases, scientific misconduct. As Carl Sagan stated, "extraordinary claims require extraordinary evidence." Accordingly, new or novel findings that purport to indicate effects that have little or no biological basis, based on the weight of the evidence coupled to first principles of relevant scientific disciplines, should be subjected to suitable reproducibility requirements, which could include causal analytics.

E. Definition of "publicly available" is needed.

EPA does not define what it means by its use of the term, "publicly available." There is more than one definition of the term currently in use by federal agencies.[16] EPA should clarify the level of access and disclosure to the public that is intended. If it intends to determine this on a case-by-case basis, that also should be made clear.

F. Greater clarity on data refinement issues is needed.

Another important aspect relevant to "public availability" is the level of data refinement EPA will require. The National Academies of Science, Engineering, and Medicine (NAS) held a workshop in 2016 to discuss obstacles for sharing data.[17] The NAS defined several key terms to ensure clarity at the workshop. EPA should consider adopting a similar lexicon to increase the clarity of its regulation. (See Table 1 in Appendix B). In addition, the NAS Report suggests a "cleaned dataset" would be acceptable to use for all routine analyses and verification. (See Table 2 in Appendix B). EPA should establish clear standards on the acceptability of "*cleaned datasets*." This will help to standardize data reporting and formatting. It will also prevent over- and under-reporting.

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[15] https://obamawhitehouse.archives.gov/omb/fedreg_final_information_quality_guidelines/

[16] Publicly available information means "any information that you reasonably believe is lawfully made available to the general public from: (i) Federal, state or local government records;(ii) Widely distributed media; or (iii) Disclosures to the general public that are required to be made by federal, state or local law." 17 CFR 160.3 [Title 17 -- Commodity and Securities Exchanges; Chapter I -- Commodity Futures Trading Commission; Part 160 -- Privacy of Consumer Financial Information]. Publicly available information is information that has been published or broadcast for public consumption, is available on request to the public, is accessible on-line or otherwise to the public, is available to the public by subscription or purchase, could lawfully be seen or heard by any casual observer, is made available at a meeting open to the public, or is obtained by visiting any place or attending any event that is open to the public. Office of the Director of National Intelligence & Office of the Director of National Intelligence, National Counterintelligence and Security Center, CI Glossary 2011.

[17] National Academies of Sciences, Engineering, and Medicine. 2016. Principles and obstacles for sharing data from environmental health research: Workshop summary. Washington, DC: The National Academies Press. doi: 10.17226/21703.

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VIII. Implementation of the Rule Should be Statute-Specific

EPA requested comment on the effect this proposed rule may have on individual EPA programs. Each of the federal environmental statutes referenced by EPA as a source for its authority to propose this rule, was enacted and designed to achieve a specific environmental goal and purpose (e.g., TSCA regulates new and existing chemicals, CAA controls air pollution on a national level, and SDWA regulates public drinking water supplies across the nation). Each statute confers its unique authority upon the agency, requiring agency review according to different scientific standards; each has its own regulations designed to effectuate the specific corresponding program's mission; and, in many cases, each statute relies on different and variable scientific disciplines. As such, ACC believes that this rule, while applicable to all the statutes identified, should be implemented by regulations specific to the objectives and scientific disciplines of each statute. ACC believes that just as the Freedom of Information Act (FOIA), which is overseen by the US Department of Justice (DOJ), is implemented by each agency with specific and separate regulations relevant to the requirements of each statute, this policy rule should be implemented by each EPA program office charged with implementing a given statute in a manner consistent with the authorities granted and requirements unique to that statute.[18]

IX. The Proposed Rule Should Apply to Enforcement and Permit Proceedings

EPA should apply the final rule to both ". . . enforcement activities or permit proceedings (including site-specific permitting actions) . . ." 83 Fed. Reg. 18768, 18771. In both these areas, EPA staff routinely use scientific evidence to make case-specific policy decisions that raise the same type of problems that occur when EPA promulgates regulations; therefore, this proposed regulation should apply to those to ensure that decisions in those areas are made appropriately.

For example, in both administrative and civil judicial enforcement programs, EPA routinely makes discretionary decisions targeting cases to pursue on the basis of scientific data on exposure of humans and ecological resources to pollutants. To do so, EPA relies on data regarding the inherent hazards of the chemical pollutants, and then estimates exposure potential and risks in a manner essentially the same as the approach EPA used to craft the regulations under the applicable environmental statute. Then, on an enforcement case-specific basis, EPA enforcement staff routinely use exposure/risk information to determine whether violations of the law (for regulatory enforcement under the CAA, CWA, RCRA, FIFRA, etc.) or releases to the environment (CERCLA, RCRA corrective action, OPA) have occurred warranting enforcement and determining the extent of sanctions and relief EPA will seek in an enforcement proceeding.

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[18] See, for example, the discussion of CWA criteria earlier in these comments under section VII. B., which is a good example of why it is important that EPA consider each statute it regulates when applying this proposed rule.

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In CAA New Source Review enforcement cases, EPA must decide whether a violation of the program occurred by constructing a "major modification" to a source by assessing whether the pollutant-specific regulatory thresholds were exceeded; analyze emissions calculations using emission factors and/or test data collected from engineering studies; and then extrapolate to the specific plant. To identify the remedial action to impose, EPA must decide which Best Available Control Technology (BACT) limits are for the modifications and that decision, in turn, requires a complex analysis of data regarding costs and efficacies of various control technologies.

In a CWA enforcement case, EPA must decide whether a facility is subject to CWA jurisdiction by determining if a discharge into a jurisdictional "waters of the United States" is subject to the National Pollutant Discharge Elimination System (NPDES) permitting and then whether the discharge violates effluent discharge requirements. If so, EPA must analyze what remedial measures are necessary, including to the receiving waters. In both the CAA and CWA cases, EPA must also prepare proposed civil penalty and pollution "mitigation" assessments, each of which require the analysis of complex economic and environmental data. This policy will require EPA to be more transparent regarding its assessment and analysis of this complex data, which is much needed.

In a CERCLA enforcement case, EPA has to decide what the removal or remedial action should be, which necessitates among other things, a site-specific risk assessment and remedial technologies selection, using a wide variety of environmental and engineering data, which should be publicly available to be verified and replicated.

Similarly, for permitting purposes under environmental statutes, EPA must routinely analyze scientific studies to decide whether to grant a permit and, if so, what conditions to impose in the permit to mitigate environmental impacts to acceptable levels. For example, in a CWA NPDES permit review, EPA determines the level of each pollutant that would be discharged to waters of the United States, whether the proposed discharge will comply with effluent limits required by technology-based effluent guidelines and water-quality standards (including Total Maximum Daily Load programs), and whether control technologies will ensure that the effluent limits will be achieved consistently. Each of those decisions requires analyzing complex environmental/engineering data on a case-specific basis.

X. Incorporate Stronger Data and Model Access Requirements into Cooperative Agreements and Grants while Complying with Privacy and Confidentiality Requirements and Laws

EPA requested comment on how EPA can incorporate stronger data and model access requirements into the terms and conditions of Cooperative Agreements and Grants. ACC believes EPA can accomplish this by implementing requirements that all models and results developed under EPA Cooperative Agreements and Grants be open access and not proprietary. EPA should also require all grant proposal applicants to include as part of any

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grant proposal a data management plan, similar to those required by the National Institutes of Health (NIH).[19] EPA may elect to exclude from these requirements grants/agreements of some specified annual amount, but that annual amount should be reasonable and ensure that the vast majority of models and results developed under grants/agreements is shared.

EPA should adopt model evaluation criteria to apply the greatest weight and credibility to models that are open access, describe the endpoint predicted clearly, are based on unambiguous open access computer algorithms, have a defined domain of applicability, have been transparently verified with publicly available datasets, and are shown to be robust and scientifically sound for the intended use.

In addition, EPA should develop common data templates and digital platforms for the most common types of research studies to be used by entities subject to Cooperative Agreements and Grants to facilitate public use and validation.

XI. The Rule Should Apply to all EPA Programs, including its IRIS Program

EPA established the Integrated Risk Information System (IRIS) in 1985 to develop and maintain a database of human health hazard assessments for chemicals. EPA's website states: "The goal of the IRIS Program was to foster consistency in the evaluation of chemical toxicity across the Agency."[20] However, the IRIS Program has been plagued for years by its slow pace generating IRIS assessments and lack of scientific transparency and reproducibility, among other deficiencies. The U.S. Government Accountability Office included IRIS in its High Risk Report, which noted that EPA has not "developed sufficient chemicals assessment information under these programs to limit exposure to many chemicals that may pose substantial health risks"[21] Although the IRIS Program has initiated changes to address some of these deficiencies, no final IRIS assessment to date reflects the full panoply of recommendations issued by the NAS in its review of the IRIS program in 2011.

Appendix C offers several specific examples of IRIS assessment that failed to reflect the best available science. We strongly recommend that the Agency apply this rule to any IRIS assessment that could be used as the basis for significant regulation.

XII. Methodologies and Technologies Providing Protected Access to Sensitive or Confidential Data

In circumstances where company CBI and other intellectual property may be implicated, EPA should confer with the CBI data owner to determine how to make that data available to the greatest extent possible without disclosing the CBI within that data, study, or model. How this is handled will likely be impacted by the type of

[19] https://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm
[20] See https://www.epa.gov/iris/basic-information-about-integrated-risk-information-system
[21] https://www.gao.gov/highrisk/transforming_epa_and_toxic_chemicals/why_did_study#t=0

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regulatory decision and statute involved.

For example, under TSCA, while the summarized study results, analysis, and final report may be publicly available, the underlying data in a health and safety study may qualify as CBI when the underlying data are not in the public domain and that data provides a commercial value to its owner.[22] In such circumstance, it is the availability of the underlying data that determines whether or not an unpublished study can be used by a competitor to support its notification or registration of a substance overseas without obtaining ownership or citation rights to use such data, depriving the data owner of the value of its investment in the underlying data. Current EPA regulations require chemical manufacturers to submit health and safety studies under some circumstances. However, it is noteworthy that none of these regulations routinely require study submitters to submit underlying data along with a final report. This indicates that the final report likely communicates sufficient information about the potential health and environmental effects to the public when a company has submitted health and safety studies in which it has a commercial interest in protecting.[23]

ACC believes that making a final study report publicly available where the underlying data are CBI would, in most circumstances, be an effective way to make relevant information publicly available about studies and data EPA may rely on, but which must be protected as CBI in circumstances triggering this policy. In these situations, EPA can access the underlying data to confirm the methods, models, and approaches are based on validated procedures, accessible data, etc. If necessary, when specialized expertise is needed, EPA could contract with an independent third-party science reviewer to confirm those findings, although we believe this would likely only be necessary in unusual circumstances. In addition, EPA might also consider an approach followed under FIFRA where Data Evaluation Records of studies are made publicly available, but not full studies.[24] Another approach is that of the European Union's REACH program, which makes Robust Study Summaries (RSS) publicly available, while protecting from disclosure the competitively sensitive underlying data of health and safety studies.

When protecting data while also promoting data access, NIH guidelines should be consulted.[25] ACC believes many of these guidelines could be applied in EPA's implementation of this proposed policy under each of the statutory programs EPA administers to ensure the guidelines adopted suit the specific needs of each statute.

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[22] See, e.g., *Cohen v. Kessler*, No. 95-6140 (D.N.J. Nov. 25, 1996).

[23] 40 C.F.R. §720.50(a)(3)(i) requires that if data do not appear in the open scientific literature, the submitter must provide a full study report, including the experimental methods and materials, results, discussion and data analysis, conclusions, references, and the name and address of the laboratory that developed the data.

[24] See, e.g., https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/pdf/010501/010501-050.pdf

[25] See https://osp.od.nih.gov/2016/05/02/protecting-data-promoting-access-improving-our-toolbox/; https://www.niaid.nih.gov/research/data-security; and https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5302472/

EPA should ensure that it implements its final rule in a manner that enables it to use confidential health records that may exist with certain kinds of studies, such as long-term air pollution and workplace exposure studies that involve confidential health records. Several agencies and organizations, in addition to NIH, have successfully addressed the issue of data access while maintaining confidentiality that should be considered by EPA. For example:

- The existing rule requiring federally funded research to be made available to other researchers. This standard could be adopted and applied to third-party funded researchers.
- Health care claims and related data are now being made available to researchers in de-identified form by some health insurance companies, such as Optum, which offers a "proprietary research database of health care and administrative data that links patient, physician, and treatment attributes from millions of geographically diverse individuals in the U.S." Optum appears to have developed methods and procedures to appropriately address confidentiality concerns.
- Medicare claims data are already available to researchers in de-identified form. Algorithms and methods developed by the Center for Medical Services should be examined by the EPA.
- Several professional societies have guidance on the protection of health data and de-identification, such as the Institute of Electrical and Electronic Engineers and the International Association of Privacy Professionals. [26]

EPA should develop clear guidance on protecting privacy, de-identifying data, and settling disputes should a breach occur. It may also want to consider establishing an office similar to that of NIH's Office of Research Integrity to adjudicate any issues that may arise in the administration of its practices under this rule.[27]

XIII. The Rule Should Generally Apply Prospectively to EPA Decision Making

ACC does not support retrospective application of the final rule in cases where the Agency follows a periodic review schedule for updating regulations, which includes review of underlying scientific assessments. Retrospective application of any regulation (and its underlying scientific evaluations) is rife with complication, confusion, and significant ambiguity for EPA and stakeholders alike. For example, each NAAQs review under the CAA is based on a substantial amount of scientific and policy information used to inform EPA's determinations of appropriate levels for each standard. The retroactive application of this proposal to those administrative records would only serve to confuse, distress, and impede a NAAQS review process that is already severely overburdened. For example, it is unclear which administrative NAAQS records would be covered by the proposal and how far back it would apply.

[26] http://www.ehealthinformation.ca/wp-content/uploads/2014/08/2010-Risk-based-de-identification-of-health-data.pdf and https://iapp.org/media/pdf/knowledge_center/Perspectives_on_Health_Data_De-Identification_final.pdf

[27] https://ori.hhs.gov/

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Without a clear statement, the proposal could potentially cover more than a decades' worth of NAAQS administrative records and scientific analyses. The value of such an application is similarly uncertain. While ACC remains supportive of increased transparency in significant regulatory actions in the future, we encourage EPA to avoid the creation of unnecessary ambiguity and burdens and refrain from the application of this proposal to previous administrative NAAQS records. ACC recommends the final rule be applied prospectively in a manner that integrates its application within the periodic review schedule established for each criteria air pollutant.

However, in cases where EPA has developed analytical tools and models, e.g., ECOSAR, in the past that incorporate dose response data, it may be valuable to apply this rule retrospectively. In other cases, such as IRIS assessments, where the Agency has yet to articulate a periodic review schedule for updating scientific assessments dating back 10-20 years or longer, EPA should develop appropriate mechanisms for application of the rule.[28]

XIV. Bias Should not be Presumed

EPA requested comment on how application of the proposal might inadvertently introduce bias regarding the timeliness and quality of the scientific information available. If EPA uses a weight-of-the-evidence approach (as required under TSCA)[29] and EPA has concerns about bias having been introduced, it can evaluate this using a sensitivity analysis by evaluating the impact of each study and/or model on the overall outcome of the analysis.[30] That said, bias should not be inferred if newer, more scientifically robust studies based on modern, up to date knowledge of biology and dose response are determined to be of better quality, relevance, and evidentiary value.

XV. EPA Should Work with Entities Where Scientific Data are not Publicly Available in a Manner Sufficient for Independent Evaluation

Where data are not available in a manner sufficient for independent evaluation, EPA should attempt to work with data owners to reach an agreement to make the information available to the public to the greatest extent practicable without

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[28] In addition, stakeholders who seek to urge EPA to undertake a retrospective review do have options at their disposal, e.g., they can develop a voluntary new evaluation under TSCA, petition EPA, or file an Information Quality Request (IQA) requesting a correction.

[29] The TSCA Risk Evaluation rule provides an excellent definition of "weight-of-the-scientific-evidence" that should be adopted across the federal government, but certainly across EPA, at a minimum. That definition is: " a systematic review method, applied in a manner suited to the nature of the evidence or decision, 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." See 82 Fed. Reg. 33726, 33733 (July 20, 2017).

[30] EPA's implementation and adherence to systematic review in the implementation of this proposal as it has committed under TSCA, will serve to guard against the introduction of bias. See EP's *Application of Systematic Review in TSCA Risk Evaluations* at https://www.epa.gov/sites/production/files/2018-06/documents/final_application_of_sr_in_tsca_05-31-18.pdf

jeopardizing the privacy, confidentiality, or the proprietary interests that deserve protection. In circumstances where there is significant difficulty making data available in a meaningful way, EPA should consider contracting with external experts in the scientific discipline at issue, have them sign confidentiality agreements, analyze the data, and prepare a confidential report with a non-confidential summary for EPA to share publicly.

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APPENDIX A: Proposed Regulatory Text

Section 30.1 What is the purpose of this subpart?
This subpart directs EPA to ensure that the regulatory science underlying its actions is publicly available in a manner sufficient for independent validation.

Section 30.2 What definitions apply to this subpart?
As used in this subpart, all terms not defined herein shall have the meaning given them in the Act or in subpart A; and the following terms shall have the specific meaning given them.

- **Dose Response data and models** – the data and models used to characterize the quantitative relationship between the amount of dose or exposure to a pollutant, contaminant, or substance and the magnitude of a measured or predicted response or health or environmental impact.

  A dose response and concentration response can be empirical, e.g., it can describe the measured relationship from experimental measurements. A response can be just a response and not an actual "impact."

- **Material Regulatory Science** – specific scientific studies and analyses that represent the best available science that, based on weight-of-the-evidence, are material to and represent the scientific basis of the requirements and/or quantitative analyses of EPA final significant regulatory decisions.

- **Regulatory decisions** – final regulations determined to be "significant regulatory actions" by OMB per EO 12866, which is defined as any regulatory action that is likely to result in a rule that may:

  - Have an annual effect on the economy of $100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health, or safety, or state, local, or tribal governments or communities;
  - Create a serious inconsistency or otherwise interfere with an action taken or planned by another agency;
  - Materially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or
  - Raise novel legal or policy issues arising out of legal mandates, the president's priorities, or the principles set forth in the Executive Order 12866.

- **Regulatory science** – scientific information, including assessments, models, criteria documents, and regulatory impact analyses that provide the basis for EPA's policies, procedures, guidance, proposed and final significant regulatory decisions.

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- **Research data** – as defined by UAR is: the recorded factual material commonly accepted in the scientific community as necessary to validate research findings, but not any of the following: preliminary analyses, drafts of scientific papers, plans for future research, peer reviews, or communications with colleagues. This ''recorded'' material excludes physical objects (e.g., laboratory samples).

  "Research data" do not include:

  (i) Trade secrets, commercial information, materials necessary to be held confidential by a researcher until they are published, or similar information which is protected under law; and
  (ii) Personnel and medical information and similar information the disclosure of which would constitute a clearly unwarranted invasion of personal privacy, such as information that could be used to identify a particular person in a research study.

Section 30.3 How do the provisions of this subpart apply?
"To dose response data and models underlying pivotal regulatory science that are used to justify significant regulatory decisions regardless of who funded it or the identity of the party conducting the regulatory science." These provisions do not apply to "physical objects (like laboratory samples), drafts, and preliminary analyses." Except where explicitly stated otherwise, the provisions of this subpart do not apply to any other type of regulatory action, including enforcement actions and permit proceedings, etc.

Section 30.4 What requirements apply to EPA's use of studies when taking final action?
EPA shall clearly identify all studies or other regulatory science relied upon when it takes any agency action and make all studies available to the public to the "extent practicable."

Section 30.5 What requirements apply to use of dose response data and models?
When promulgating significant regulatory actions, the Agency shall ensure that the dose response data and models underlying pivotal regulatory science are publicly available in a manner sufficient for independent validation, **verification,** and analysis.
This may include:

- Data (where necessary, could be subject to access and use restrictions)
- Associated protocols
- Computer algorithms and models[31]
- Recorded factual materials
- Detailed descriptions of how to access and use such information

But in a manner consistent with law, protects privacy, confidentiality, CBI, and is sensitive to national and homeland security.

[31] We suggest substituting "algorithms" in place of "codes" because specific computer codes can be proprietary.

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Information is "publicly available in a manner sufficient for independent evaluation" when it includes the information necessary for the public to "understand, assess, and replicate findings."

Section 30.6 What additional requirements pertain to the use of dose response and models underlying pivotal science?
EPA shall describe and document any assumptions and methods used and should describe variability and uncertainty. EPA shall evaluate the appropriateness of using default assumptions, including assumptions of a linear, no-threshold response, on a case-by-case basis. EPA shall clearly explain scientific basis for each model assumption used and present analyses showing the sensitivity of the modeled results to alternative assumptions. When available, EPA shall give explicit consideration to high-quality studies that explore: a broad class of parametric dose-response or concentration-response models; a robust set of potential confounding variables; nonparametric models the incorporate fewer assumptions; various threshold models across the dose or exposure range; and models that investigate factors that might account for spatial heterogeneity.

Section 30.7 What role does independent peer review [have] in this section?
EPA shall conduct independent peer review on all pivotal regulatory science used to justify regulatory decisions, consistent with OMB Final Information Quality Bulletin for Peer Review (70 FR 2664) and the exemptions therein apply. EPA will ask peer reviewers to articulate the strengths/weaknesses of EPA's justification for assumptions applies and the implications of those assumptions for the results.

Section 30.8 How is EPA to account for cost under this subpart?
EPA shall implement the provisions of this subpart in a manner that minimizes costs.

Section 30.9 May the EPA Administrator grant exemptions to this subpart?
Yes. The Administrator may grant an exemption to this subpart on a case-by-case basis if he or she determines that compliance is impracticable because:
(a) It is not feasible to ensure that all dose response data and models underlying pivotal regulatory science is publicly available in a manner sufficient for independent validation, in a fashion that is consistent with law, protects privacy, confidentiality, confidential business information, and is sensitive to national and homeland security; or
(b) It is not feasible to conduct independent peer review on all pivotal regulatory science used to justify regulatory decisions for reasons outlined in OMB Final Information Quality Bulletin for Peer Review (70 FR 2664), Section IX.

Section 30.10 What other requirements apply under this subpart?
EPA shall implement the provisions of this section consistent with the definition of ''research data'' in Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards, exemptions in Public Law 89–487, and other applicable federal laws. Where appropriate, data sharing agreements and state-of-the-art data-masking techniques may be employed to facilitate access to information.

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ACC notes here its support for the text of Public Law 89-487, which is incorporated by reference in Section 30.10 provides the following exemptions are applicable to this proposed regulation:

1) Specifically required by Executive Order to be kept secret in the interest of national defense or foreign policy;
2) Related solely to the internal personnel rules and practices of any agency;
3) Specifically exempted from disclosure by statute;
4) Trade secrets and commercial or financial information obtained from any person and privileged or confidential;
5) Inter- or intra-agency memorandums or letters which would not be available by law to a private party in litigation with the agency;
6) Personnel and medical files and similar files the disclosure of which would constitute a clearly unwarranted invasion of personal privacy;
7) Investigatory files compiled for law enforcement purposes except to the extent available by law to a private party;
8) Contained in or related to examination, operating, or condition reports prepared by, on behalf of, or for the use of any agency responsible for the regulation or supervision of financial institutions; and
9) Geological and geophysical information and data (including maps) concerning wells.

Where appropriate, data-sharing agreements and data-masking techniques may be used.

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APPENDIX B: Definitions of NAS Principles

Definitions in NAS Principles and obstacles for sharing data from environmental health research: Workshop summary.
Definition: meta-analysis *Meta-analysis* is a way of quantitatively combining data from many different studies using a statistical process.
Definition: reanalysis The term "*reanalysis*" is defined as conducting further analyses of the exact same data to determine if the same results are obtained and may include use of the same programs and statistical methodologies that were originally used to analyze the data or may use alternative methodologies.
Definition: replication The term "*replication*" is the repetition of a scientific experiment or a trial using exactly the same protocols and statistical programs but with data from a different population to determine if consistent results are obtained with data from a different population.
Definitions: reproduction The term research "*reproduction*" refers to an experiment conducted to addresses the same research question as the original work, but examines the question from a different angle.
Definition: raw data The term "raw data" is defined as the unmodified or unprocessed data that is obtained directly from a survey or experiment (modified from NAS, 2016 P6)
Definition: cleaned-up data *Cleaned-up data* consist of the raw data modified to remove obvious errors.
Definition: processed data The term "processed data" refers to information that has been computed and analyzed to extract relevant information (NAS, 2016), and may include: • Aggregation – combining multiple pieces of data. • Analysis – collection, organization, analysis, interpretation and presentation of data • Classification – separation of data into various categories. • Reporting – list detail or summary data or computed information. • Sorting – the arrangement of items in some sequence and/or in different sets. • Summarization – reducing detail data to its main points. • Validation – Ensuring that supplied data is correct and relevant. (wiki https://en.wikipedia.org/wiki/Data_processing)
Definition: final clean data set

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The term "*final clean data set*" is the information provided with a scientific publication (modified IOM, 2016 P6)
Definition: metadata *Metadata* is a set of data that describes other data

TABLE 2 – Data flow from NAS Report

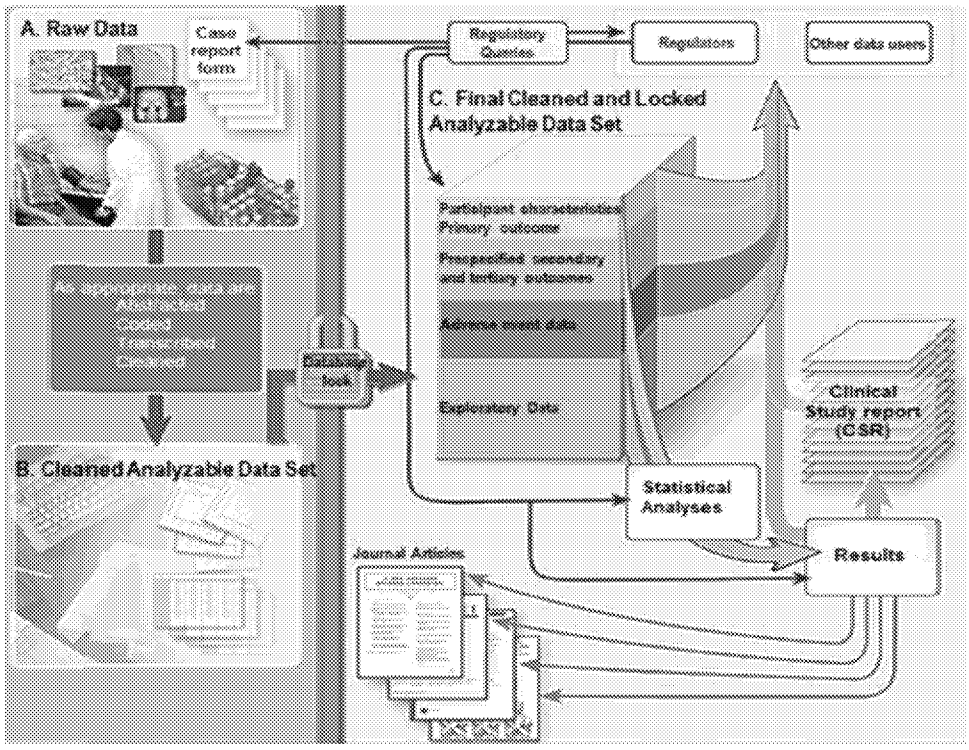

FIGURE 2-1 Data flow from participant to analyzed data and reporting.
SOURCE: IOM, 2014.

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APPENDIX C: Chemical-Specific Case Studies

Case Study 1: Trimethylbenzenes (TMBs)

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 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.

The IRIS assessment of TMBs does not accurately represent the health effects associated with exposure to TMBs because it 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.

Case Study 2: Formaldehyde

Formaldehyde occurs naturally in every living system – from plants to animals to humans – all of which produce formaldehyde as a normal part of metabolism. In addition, its unique and versatile chemical properties make it a common and beneficial part of modern life. Formaldehyde has been the subject of extensive and robust scientific inquiry. EPA has been involved in assessing the human health risk of formaldehyde since the late 1970s. Large numbers of epidemiology, toxicology and biomechanical studies have informed the science surrounding formaldehyde, so that there a rich body of data exists.

The most recent draft Integrated Risk Information System (IRIS) formaldehyde assessment (2010) proposed exposure limits so low that the trace levels of formaldehyde found in human breath would present a cancer risk. The 2010 draft assessment also noted that: *"Human epidemiological evidence is sufficient to conclude a causal association between formaldehyde exposure and nasopharyngeal cancer, nasal and paranasal cancer, all*

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leukemias, myeloid leukemia and lymphohematopoietic (LPH) cancers as a group." The National Academy of Sciences (NAS) then conducted a peer review of this draft and issued its final report in April 2011. The NAS report was critical of the draft IRIS assessment---an assessment that the IRIS program took 12 years to develop.

The NAS stated that EPA's claims regarding all leukemias, myeloid leukemia or related hematopoietic cancers were not supported. It noted that EPA's preliminary conclusions appeared subjective and that no clear scientific framework had been used by EPA to reach its conclusion. The NAS recommended that EPA revisit its determination of causality for specific LHP cancers, using methodology that integrates lines of evidence and addresses the specific criticisms in the NAS report. The NAS also made numerous recommendations for the improving the overall process and application of science used in all assessments generated by the IRIS program. Now, seven years since that NAS report was published, EPA continues to revise its assessment while not disclosing how emerging scientific evidence or modern risk assessment methods are being employed.

Meanwhile, newly published research based on the recommendations in the NAS report has advanced the state of the science. Raw data (made available after multiple years of FOIA requests) from studies conducted by the Federal government ---and upon which EPA relied on for its previous assessment conclusions--- were re-analyzed and the findings contradicted the original study conclusions. Today our knowledge regarding formaldehyde is much greater; yet it does not appear that this new knowledge has been applied in the EPA's assessment of formaldehyde risk. Published research demonstrates that inhaled formaldehyde cannot reach the bone marrow where leukemia occurs and that safe thresholds for formaldehyde exposure exist. This formaldehyde case study is an example of the long-term problems with the lack of consistent, transparent application of modern scientific knowledge regarding chemical exposures and human health risk.

Case Study 3: Ethylene Oxide

The Integrated Risk Information System (IRIS) assessment of ethylene oxide (EO) originated with a carcinogenicity assessment in 1985. The first comprehensive draft was published in 1998. An external review draft was issued in 2006, followed by a Science Advisory Board (SAB) review in 2007. Revisions of the EO assessment were made in 2011 and 2013, and an additional SAB review was conducted in 2014-2015. The final IRIS assessment for EO was posted in December 2016.

Using unsupportable and un-reviewed conservative risk assessment modeling, the IRIS assessment concludes that the one-in-a-million lifetime cancer risk value associated with exposure to EO is less than 1 part per trillion (ppt). This value is far below both EO background levels 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 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 the

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IRIS Program did not systematically integrate all of the evidence. Public comments on the EO IRIS assessment can be found in Docket No. EPA-HQ-ORD-2006-0756.

EO has dozens of important applications, including the manufacture of ethylene glycol based antifreeze, aircraft deicers, and PET plastics. EO is also used to produce higher-value derivatives such as ethoxylates, ethanolamines, glycol ethers, and polyether polyols. A small but critical use of EO is for the sterilization of medical equipment.

EPA's SAB 2007 review concluded that substantial revisions were needed to the draft IRIS assessment including:

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

Meeting materials, including public comments, can be found at https://yosemite.epa.gov/sab/sabproduct.nsf/MeetingCal/7E3E313F627541D78525711400470D01.

The 2015 SAB Committee that reviewed the revised 2013 EO draft IRIS assessment did not conduct an independent, unbiased review. Problems included:

- Several SAB members made inaccurate public statements indicating industry produced scientific studies should be not be considered due to potential industry influence, although no evidence of biased data sponsored by industry was ever presented.
- SAB members did not understand new evidence-based medicine concepts regarding mutagenicity of cancer cells and the contribution of naturally occurring EO in DNA repair mechanisms.
- The SAB recommended using epidemiology data sets with questionable or scientifically unsound characteristics to estimate cancer risk and rejected alternative data sets that are as or more robust than those selected.

EPA still did not use individual data for modeling as recommended by the SAB in 2007, and did not adequately explore alternatives to the linear low dose modeling approach.

Meeting materials, including public comments, can be found at https://yosemite.epa.gov/sab/sabproduct.nsf/MeetingCal/17F305EC43EB1A6585257E2D0050255F.

The IRIS Program used a spline approach (piecewise linear model that was not presented during either SAB review) for exposure-response analyses for each of the lymphoid and breast cancer endpoints and ultimately combined the results. This approach results in higher risk at lower exposure levels and leads to proposed regulatory levels that are orders of magnitude lower than what the epidemiologic and genotoxicity scientific evidence would support.

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Further, the IRIS Program did not fully consider all available evidence in finalizing the EO assessment. Scientific evidence clearly indicates that EO is a weak mutagen and a unit risk factor of less than 1 ppt is not realistic or reliably measurable, and is orders of magnitude lower than levels of EO in ambient air and the normal, endogenous levels of EO present in human bodies. Moreover, the assessment fails to consider the difference between exposures to EO produced outside the human body and exposure to EO produced within the human body as a normal metabolic product.

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