UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

September 30, 2020

EPA-SAB-20-012

The Honorable Andrew Wheeler
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

Subject: Science Advisory Board (SAB) Consideration of the Scientific and Technical Basis of EPA's Proposed Rule titled "Increasing Consistency and Transparency in Considering Benefits and Costs in the Clean Air Act Rulemaking Process."

Dear Administrator Wheeler:

As part of its statutory duties, the EPA Science Advisory Board (SAB) may provide advice and comments on the scientific and technical basis of certain planned EPA actions pursuant to the Environmental Research, Development, and Demonstration Authorization Act of 1978 (ERDDAA). ERDDAA requires the EPA to make available to the SAB proposed criteria documents, standards, limitations, or regulations, together with relevant scientific and technical information on which the proposed action is based. On the basis of this information, the SAB may provide advice and comments. Thus, the SAB is submitting the attached report on EPA's Proposed Rule titled "Increasing Consistency and Transparency in Considering Benefits and Costs in the Clean Air Act Rulemaking Process" published in the Federal Register on June 11, 2020 (85 FR 35612-35627). In developing this report, the SAB followed the engagement process for review of regulatory actions outlined in your memo of February 25, 2020.

The Proposed Rule establishes procedural requirements governing the development and presentation of benefit-cost analyses (BCA) for significant rulemakings conducted under the Clean Air Act (CAA) to ensure consistency and transparency. The Proposed Rule requires that EPA: (1) prepare a BCA for all significant CAA proposed and final regulations; (2) adhere to best practices for the development of the BCA; and (3) provide a transparent presentation of the BCA results in the rule preamble.

The SAB met by video conference on August 11, 2020, and September 15, 2020. Members reviewed the scientific and technical basis of the Proposed Rule. The SAB's advice and comments are provided in the enclosed report and summarized below.

In general, the SAB urges EPA to consider carefully which aspects of BCA should be included in the final rule versus which aspects should be in guidance, given the case-by-case nature of BCA. The SAB finds that implementation of the Proposed Rule as written would be problematic, and that incorporating

our scientific and technical recommendations would result in BCA that is more defensible and likely to be more informative to policy makers.

The SAB's other major recommendations and comments on the Proposed Rule are as follows:

- EPA should revise the requirements for estimation of benefits to incorporate systematic review approaches, better define causality, and include effects for which causal or likely causal relationships may be less certain.
- EPA should revise the requirements for selection of health endpoints to provide greater clarity and transparency, especially with regard to the selection of concentration response functions.
- EPA should revise the requirements for uncertainty analysis to indicate that the scope and depth of the analysis should be appropriate for the context.
- EPA should revise the rule to better incorporate low probability, high-consequence hazards, and to make clear when unquantified benefits and costs could be significant. Correctly characterizing the full range of possible outcomes is important: BCA is a tool to help policy makers and the public understand the consequences of a proposed action, not a decision rule in itself.

The SAB appreciates the opportunity to provide the EPA with advice and comment on the Proposed Rule. We look forward to receiving the Agency's response.

Sincerely,

/s/

Dr. Michael Honeycutt, Chair
Science Advisory Board

Enclosure

NOTICE

This report has been written as part of the activities of the EPA Science Advisory Board, a public advisory committee providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide balanced, expert assessment of scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency and, hence, the contents of this report do not represent the views and policies of the Environmental Protection Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute a recommendation for use. Reports of the EPA Science Advisory Board are posted on the EPA website at http://www.epa.gov/sab.

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Science Advisory Board (SAB) Consideration of the Scientific and Technical Basis of EPA's Proposed Rule titled "Increasing Consistency and Transparency in Considering Benefits and Costs in the Clean Air Act Rulemaking Process."

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ACRONYMS AND ABBREVIATIONS

BCA	Benefit-Cost Analysis
CAA	Clean Air Act
CCS	Congestion Charging Scheme
C-R	Concentration-Response
EO	Executive Order
HEI	Health Effects Institute
IRIS	Integrated Risk Information System
ISA	Integrated Science Assessment
LEZ	Low Emissions Zone
MOA	Mode of Action
NAAQS	National Ambient Air Quality Standards
NASEM	National Academy of Sciences, Engineering and Medicine
OMB	Office of Management and Budget
SAB	Science Advisory Board
TSCA	Toxic Substances Control Act
U.S. EPA	U.S. Environmental Protection Agency
WoE	Weight of Evidence

1. INTRODUCTION

The EPA's Proposed Rule titled "Increasing Consistency and Transparency in Considering Benefits and Costs in the Clean Air Act Rulemaking Process" was published on June 11, 2020 in the Federal Register (Environmental Protection Agency, 2020). The Proposed Rule would establish procedural requirements governing the development and presentation of benefit-cost analyses (BCA) for significant rulemakings promulgated under the Clean Air Act (CAA). The SAB is offering comments on the extent to which the provisions in the Proposed Rule are consistent with best available scientific information and in accordance with best practices from the economic, engineering, physical, and biological sciences.

The Proposed Rule establishes procedural requirements governing the development and presentation of benefit-cost analyses (BCA) for significant rulemakings conducted under the Clean Air Act (CAA) to ensure consistency and transparency. The Proposed Rule requires that EPA: (1) prepare a BCA for all significant CAA proposed and final regulations; (2) adhere to best practices for the development of the BCA; and (3) provide a transparent presentation of the BCA results in the rule preamble.

In developing this report, the SAB followed the engagement process for review of regulatory actions outlined in Administrator Wheeler's memo of February 25, 2020 (Wheeler, 2020). The SAB met by video conference on August 11, 2020, and September 15, 2020. Members reviewed the scientific and technical basis of the Proposed Rule. Oral and written public comments were considered throughout the advisory process. The SAB's advice and comments follow below, organized by topics that arose from the SAB's deliberations.

In developing this report, the SAB was mindful that the Proposed Rule sought to codify practices outlined in existing peer reviewed guidance documents, including the EPA's *Guidelines for Preparing Economic Analyses* (Environmental Protection Agency, 2010, Updated 2014). At the time of this writing, the *Guidelines* are undergoing a periodic update and the SAB Economic Guidelines Review Panel (SAB-EGRP) is reviewing the revisions contained in this update. Hence, the SAB sought to limit its review to requirements in the Proposed Rule that would not be addressed by the SAB-EGRP. Further SAB advice will be available with the completion of the SAB-EGRP's report and its approval by the chartered SAB.

2. SAB ADVICE AND COMMENTS ON THE PROPOSED RULE

2.1 Definitions

Section 83.1 of the Proposed Rule provides definitions of terms used in regulatory assessments. In the text below, the SAB provides some suggestions for improvement in the definitions. The first sentence in the first bullet below is adapted from OMB Circular A-4. The second sentence explains the BCA should use opportunity costs (as opposed, for example, to accounting costs) and that benefits should be derived from willingness-to-pay estimates from domestic individuals (as opposed to international interests). The third sentence directly references what is in the current proposed rule draft.

- Benefit-Cost Analysis – The SAB recommends revising the definition of BCA in the Proposed Rule to clearly state that BCA provides decision makers with a clear indication of the most efficient alternative, that is, the alternative that generates the largest net benefits (benefits minus costs) to society (ignoring distributional effects) (Office of Management and Budget, 2003). The definition should indicate that costs should be opportunity costs and benefits represent the willingness-to-pay for a policy outcome valued by United States individuals. The definition should also indicate that BCA addresses the question of whether the benefits for those who gain from the action are sufficient to, in principle, compensate those burdened such that everyone would be at least as well off as before the policy. The SAB recognizes that there are important foundational issues in BCA, such as the Scitovsky critique of the Kaldor-Hicks compensation criterion, that we do not address here. See, for example, Price (1977).

- Regulatory options – In this section, the current text advises economists to provide regulatory options that are both more and less stringent in addition to the option currently being considered for implementation. However, for benefit-cost analysis, as opposed to cost-effectiveness analysis, the regulatory options should only help to solve a problem, not accomplish a goal or objective. For example, a less stringent option might accomplish less but at lower cost. Therefore, the SAB recommends that the following parts of the definition of regulatory options be revised as indicated below:

  "(2) From "A more stringent option which accomplishes the stated objectives of the Clean Air Act…" to "A more stringent option which *contributes to* the stated objectives of the Clean Air Act and that achieves additional benefits (and presumably costs more) beyond those realized by the proposed or finalized option; and"

  "(3) from "A less stringent option which accomplishes the stated objectives of the Clean Air Act…." to "A less stringent option which *contributes to* the stated objectives of the Clean Air Act and that costs less (and presumably generates fewer benefits) than the proposed or finalized option."

2.2 Estimating Benefits

Section 83.3(a)(7) establishes requirements for the selection of benefit endpoints. In the text below, the SAB is offering its comments on the requirement that the Agency must select endpoints for which the scientific evidence indicates there is a clear causal or likely causal relationship between pollutant exposure and effect. The SAB is also offering recommendations for how to establish criteria for a

weight of evidence (WoE) determination on causality that would be appropriate to apply to all benefit endpoints.

Several scientific issues are raised by the text of this section including: (1) whether benefits analyses for effects should be limited to those described as having a clear or likely causal relationship, and (2) what best practices can and should be applied to evaluate causality.

2.2.1 Benefits analyses for effects that are clearly causal or likely causal

It is essential for analyses to characterize health effects for which the science indicates the greatest likelihood that changes in exposure would provide positive benefits. The focus on clearly causal or likely causal relationships provides a useful analysis. If feasible, inclusion in the benefits analyses of effects for which the relationship may be less certain (e.g., possibly causal), but the impact would be substantial, could provide a more complete perspective accounting for uncertainties (McGartland, et al., 2017). Modification of the language in Section 83.3(a)(7) should allow such analyses, while the current language appears to exclude them.

It remains unclear what specific criteria the Agency will use to determine causality. The Agency should transparently include in the rule, or reference, relevant guidance which provides clear definitions for causal determinations, e.g., "causal" or "likely causal," based on current best Agency practices. The Agency should also explain what types of scientific evidence are needed to justify a particular causal determination (i.e., epidemiology, animal toxicology data, and mechanistic biology results should be considered). For example, the Agency has clear definitions that it uses in the development of its Integrated Science Assessment (Environmental Protection Agency, 2015). Additionally, the Agency should make clear the distinction between association vs. causation given that most epidemiological studies are by nature observational rather than experimental and thus there could be several potential reasons for an observed association that need to be evaluated before an inference can be made to support a cause-effect relationship.

While cancer effects and a range of endpoints in Integrated Science Assessments (ISAs) are routinely characterized for their likelihood in humans, this is not generally done for many noncancer health effects for chemicals not assessed with ISAs. Analyses for these chemicals and endpoints have been described to permit characterization of the health risks arising from them (Clewell and Crump, 2005). Including these endpoints would strengthen the benefits analyses.

2.2.2 Systematic Review Framework

One approach for determining if there is a clearly causal or likely causal relationship is systematic review. A systematic review is a structured process of identifying, evaluating, and integrating evidence for the question under evaluation. Careful specification of the question to be addressed is essential to the utility of the systematic review. Prior to the start of the review, a protocol is written to describe the methodology for searching for studies, determining if each study meets a predefined formulation defining the Population studied, the Exposure considered, the Comparator, and the Outcome (PECO). Criteria are determined prior to conducting the analysis for consistent evaluation of studies and an a priori framework for synthesizing and integrating studies is developed to determine the strength of the evidence. When done correctly, the systematic review process increases transparency and reduces bias in decision making.

EPA has developed a method for systematic reviews within the Integrated Risk Information System (IRIS) program. That approach has been reviewed fairly favorably by the National Academy of Sciences, considering both the overall process (National Academies of Sciences, Engineering and Medicine, 2018), and when considering one specific example (National Academies of Sciences, Engineering and Medicine, 2019). However, the National Academies of Sciences Engineering and Medicine (NASEM) continue to have some suggestions for improving the systematic reviews conducted in IRIS, and the EPA should continue to improve the process based on the NASEM suggestions. The EPA has also developed an approach to applying systematic review to its Toxic Substances Control Act (TSCA) risk evaluations (Environmental Protection Agency, 2018) which is currently undergoing review by the NASEM. Should the TSCA approach also be favorably reviewed, these represent two Agency processes that could be adapted, as needed, for this regulation. Additionally, if a systematic review has already been conducted for a specific pollutant and health endpoint, EPA may be able to be use it directly. The EPA may want to set standards for acceptable systematic reviews.

For TSCA, EPA has adopted the definition - ‘‘Weight of the scientific evidence means 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’’ (Environmental Protection Agency, 2017). This definition is appropriate for the Clean Air Act as well in addressing causality.

The Agency utilizes a weight of evidence framework for causal determination in its ISAs which includes: a description of the types of scientific evidence used in making determinations on causality; the key aspects of the evidence evaluation needed to reach causality conclusions; as well consideration of uncertainty. This approach is not dissimilar to a systematic review, and most of the principles within the existing framework could be translated to a systematic review framework. A 2017 publication by Owens et al. also summarizes a framework for assessing causality. These aspects should be incorporated or referenced in the Proposed Rule, and the criteria for integrating evidence from epidemiologic, controlled human exposure, and animal toxicological studies (including mode of action data) should be key elements. This process should focus on evaluating the quality of evidence (i.e., human relevancy and adequate exposure characterization to determine effects) and the consistency in the pattern of effects as well as the strengths, limitations, and uncertainties in the overall evidence. Currently, the Proposed Rule’s discussion of concentration-response relationships only focuses on epidemiology studies and makes no reference to other relevant scientific data that could inform the determination (e.g., animal studies).

2.2.3 Evaluating causality

There are number of methodologies for evaluating exposure to a chemical and the likelihood of a particular disease in humans, i.e., what is the evidence that the relationship is causal? In addition, the available scientific data characterizing aspects of this relationship include epidemiological studies, whole animal toxicology and biology studies, and in vitro studies utilizing a wide range of sources of biological materials including tissues, cells, or purified macromolecules. Less frequently, controlled human studies (e.g., chamber studies with air pollutants) are available. Methods for evaluating causality using specific study types tend to be most strongly developed while characterization across data types is still ongoing though essential to provide a complete perspective. SAB members have a range of perspectives on methods for evaluating and describing causality that are described here.

2.2.4 Evaluation of causality in epidemiology

One of the first approaches, presented as a list of postulates, was developed by Sir Bradford Hill in 1965 (Hill, 1965), and was based on the U.S. Surgeon General's report regarding cigarette smoking and lung cancer. While the Hill list of postulates relied heavily on findings from epidemiology studies as part of the causality framework, it also considered biological plausibility, which meant that findings from epidemiology studies should be biologically plausible, e.g., similar health effects were observed in animal studies in a dose-dependent manner. Since 1965, further approaches to assess causality (Weed, 2005; Rhomberg et al., 2011) have been developed. These analyses provide greater clarity on the importance of a reliable mode-of-action[1] (MOA) explanation of findings from human studies. Sources of MOA understanding typically include findings from animal, in vitro and in silico studies. In addition to providing insight on causality, MOA also provides insights on the dose-response relationship, e.g., whether there is a threshold and at what dose such threshold might exist. In the case of a threshold, causality is not absolute, but is dose-dependent. While a MOA understanding is relevant to a causality determination, it becomes particularly important for chemicals with relatively limited epidemiological data sets. As part of a causality determination, EPA should explicitly present a clearly articulated and comprehensive MOA mode-of-action analysis, which considers the plausibility of different MOAs, identifies the best-supported MOA, and describes the potential for dose-dependent causation.

2.2.5 Statistical causal analyses

Section 83.3(a)(7) of the Proposed Rule calls for selection of endpoints for which there is scientific evidence of a clear causal (or likely causal) relationship between exposure and effect. While this is reasonable, there is no "one size fits all" approach to causality; and a variety of approaches may need to be taken.

In recent years, there has been an enormous statistical literature on the theme of "causal inference," for example, see the classical treatise of Pearl (2009) or the very recent monograph of Hernan and Robins (2020). Some serious efforts have been made to apply these methods to determine the impact of NAAQS standards on health, and the Health Effects Institute (HEI) has sponsored several research programs, often under the title "Accountability," in which they have tried to make a direct assessment of the effect of interventions, sometimes called natural experiments, on air pollution and human health. Reports arising from HEI studies include: Peters, et al., (2009); Peel, et al. (2010);Kelly, et al.(2011a, 2011b); Noonan, et al.(2011); Wong, et al. (2012); Morgenstern, Harrington, and Shih, (2012); Zhang, et al., (2013); Dockery, et al. (2013); Zigler, et al. (2016); Gilliland, et al. (2017); and Russell, et al. (2018). Possibly the original study of this nature was conducted by Pope (1991), who examined the effect on particulate matter (PM10) and hospital admissions during a shutdown over several months of a steel mill in Utah, arguing convincingly that both PM10 and hospitalizations decreased during this period. However, attempts to reproduce this kind of result in a variety of alternative contexts have had a mixed record of success.

[1] An MOA analysis involves a description of likely key biological events that lead to adverse health effects as a result of chemical exposure. MOA analysis was first applied to cancer risk assessment, but has subsequently been applied to other health effects. See, for example, Wiltse and Dellarco, (2000); Sonich-Mullin, et al., (2001); Meek, et al., (2003); Seed, et al., (2005); Boobis, et al., (2006); Boobis, et al., (2008); Meek, et al., (2013).

Peel et al. (2010) examined effects on air pollution and emergency department visits of traffic control measures imposed during the Atlanta Olympic Games in 1996. They noted a reduction in levels of ozone during the Games, but this was also observed at other locations and may have been due to meteorological changes rather than the traffic control measures. They noted a reduction in emergency department visits for upper respiratory infections for all age groups and for pediatric ages during the Olympic Games, but they could not confirm the conclusion of an earlier study that the number of pediatric emergency care visits for asthma was substantially reduced during the Olympic Games. HEI noted that the low overall numbers of emergency room admissions and the short duration of the traffic control measures were limitations to obtaining stronger results in this type of study.

Zhang et al. (2013) looked at the effect of control measures that were designed to reduce air pollution during the 2008 Beijing Olympic Games. They took measurements of a series of air pollutants both before, during and after the Games, and also measured a series of biomarkers in a group of young and healthy volunteers. Overall, they found reductions during the Games in several air pollutants, followed by increases again after the Games had concluded, though ozone did not follow this pattern. They also showed that these air pollution reductions matched improvements in most biomarkers, though not all. The HEI Review Committee noted that the study design did not allow the air pollution reductions to be specifically attributed to the control measures, and also noted the absence of a control sample. A further comment is that since the effects were measured through biomarkers in healthy adults, they cannot be directly related to more serious mortality and morbidity outcomes in susceptible populations.

Two studies by Kelly and co-authors (2011a, 2011b) looked at effects of pollution control measures in London, specifically the Congestion Charging Scheme (CCS) and the Low Emissions Zone (LEZ). The CCS study (Kelly et al., 2011a) showed potential reductions in air pollution but they were not large reductions, and difficult to attribute specifically to the CCS. The LEZ study (Kelly et al., 2011b) was a baseline study carried out in advance of the actual regulation, that examined the potential for detecting air pollution reductions and also for linking them to medical records. However, again the study had difficulty demonstrating clear effects and pointed to confidentiality difficulties linking the air pollution reductions to medical outcomes.

Dockery et al. (2013) re-analyzed data from an earlier study on regulatory actions to ban the use of coal in twelve Irish cities. An earlier study had concluded that these actions led to significant reductions in total mortality as well as cardiovascular and respiratory mortality. However, when the data were re-analyzed including comparison cities where the coal bans were not enforced, they concluded that only for respiratory mortality was there a statistically significant decrease. HEI concluded that "the study illustrates the considerable challenges faced by this type of analysis in eliminating biases that can lead to either overestimation or underestimation of the effects of an intervention on public health."

Among the more convincing recent studies have been the papers of Zigler and co-authors (2012, 2016, 2018) that tried to correlate EPA interventions, i.e., the designation of certain counties or zones as non-attainment areas under the NAAQS, with improvements in health outcomes in those zones. In particular, the paper by Zigler et al. (2018) won the prestigious 2019 Rothman Epidemiology Prize for its lead author. However, even that paper stopped short of a clear-cut claim of causality between air pollution control measures and health benefits:

> "Results: We found that, on average across all retained study locations, reductions in ambient PM2.5 and Medicare health outcomes could not be conclusively attributed to the nonattainment designations against the backdrop of other regional strategies that impacted the entire Eastern

United States. A more targeted principal stratification analysis indicates substantial health impacts of the nonattainment designations among the subset of areas where the designations are estimated to have actually reduced ambient PM2.5 beyond levels achieved by regional measures, with noteworthy reductions in all-cause mortality, chronic obstructive pulmonary disorder, heart failure, ischemic heart disease, and respiratory tract infections."

It is established that there are technical difficulties in applying causal inference technology to this kind of problem. For example, one common assumption made in causal inference is that of no interference between observational units (also known as the Stable Unit Treatment Value Assumption or SUTVA), but this is typically not satisfied in the air pollution context, because control measures in one locality typically affect the air quality in surrounding areas as well (Zigler et al., 2012).

This kind of discussion should not be interpreted as meaning that there is no causal effect, but a formal proof of causality by statistical methods raises many challenges. In contrast, EPA has for many years relied on a weight of evidence approach, which has limitations for formal proof of causality but is accepted by many scientists. A critique of the weight of evidence approach may be found in Cox and Popken (2020). Another SAB member has provided criticisms of observational studies (Young, and Karr, 2011; Young, et al., 2017; Young, 2017).

The SAB's recommendation is that EPA should always take causality into account when evaluating epidemiological evidence, and should especially welcome applications of the statistical field of causal inference, but should also recognize that there is no "one size fits all" approach to causality, and a variety of approaches may need to be taken.

One SAB member provided an additional perspective on causation as follows. For this member, the relevant type of causation is manipulative (or interventional) causation: Do interventions in fact make preferred outcomes more probable? This is implied by, but weaker than, mechanistic causation; and it is stronger than (and does not imply) association-based (Bradford-Hill) causation (Cox, 2018). Relevant evidence for establishing clear causal or likely to be causal exposure concentration-response (C-R) relationships includes interventional studies and quasi-experiments with suitable comparison groups. Manipulative causality cannot be established by associations in observational studies alone (e.g., by regression models, burden-of-disease models, attributable risk and probability of causation calculations, relative risks greater than 2, etc.) (Pearl, 2009). For this SAB member, the current weight of evidence framework used in the National Ambient Air Quality Standards (NAAQS) reviews does not address manipulative causation and it should be replaced by a framework that does (Cox, 2019). The current weight of evidence framework attempts to use qualitative criteria to classify evidence of causation. But evidence is continuous, and any classification system has somewhat arbitrary boundaries (and, in the present system, ambiguous boundaries). Unambiguous quantitative assessments of evidence for causality should be used instead (Cox, 2020).

2.2.6 Findings and Recommendations on Estimating Benefits

- The SAB finds that systematic review principles and approaches provide a transparent and rigorous approach that should be clearly supported in the Proposed Rule.

- The SAB finds that no "one size fits all" approach to causality should be mandated because a variety of approaches may need to be taken.

- The SAB recommends that EPA modify the language in Section 83.3(a)(7) of the Proposed Rule to allow inclusion in the benefits analyses of effects for which causal or likely causal relationships may be less certain, but the impact would be substantial.

- The SAB recommends that the Proposed Rule include reference to and support for relevant guidance from current best Agency practices. Relevant guidance includes the systematic review approaches developed for the IRIS or TSCA programs and the weight of evidence framework used in the Integrated Science Assessments. Such guidance includes noncancer health effects in the benefits analyses as well as the multiple sources of relevant scientific data (e.g., animal studies, controlled human exposure studies, toxicological studies, including mode of action) in addition to epidemiological data.

2.3 Health Endpoints

Section 83.3(a)(9) of the Proposed Rule includes proposed requirements pertaining to how the Agency will select concentration-response relationships from the scientific literature for use in quantifying health endpoints in a BCA. In the text below, the SAB offers comments on these requirements and makes recommendations for improvements to the Proposed Rule regarding how concentration-response functions should be selected for use in a benefit-cost analysis.

The SAB finds many of the requirements in this section of the Proposed Rule to be vague and lacking sufficient detail that could impact effective implementation in the BCA. The Proposed Rule also provides limited rationale regarding the scientific basis of various provisions. Overall, the SAB recommends that this section of the Proposed Rule be revised to provide transparency and clarity regarding: (1) the rationale used to select health endpoints that would be evaluated for a determination of "causal" or "likely" causal; (2) the requirements in Section 83.3(a)(9)(ii) through Section 83.3(a)(9)(vii) related to suitable study attributes for determining human health impact; (3) how the Agency will ensure consistency with and incorporation of systematic review approaches that have been recommended by the National Academies of Sciences, Engineering and Medicine and the Science Advisory Board; as well as those under development by the EPA in the consolidated Human Health Toxicity Assessment guidelines; and (4) whether any or all of these proposed requirements will be applied across all air pollutants when there are significant regulations. The SAB has provided additional detail related to each of these areas below and recommends that EPA provide more objective and transparent definitions associated with the requirements.

2.3.1 The rationale for health endpoint selection for causality determination

While the Proposed Rule recommends performing a causality determination and quantifying benefits for those health endpoints with a "causal" or "likely causal" determination, it does not provide sufficient detail on the selection of specific health endpoints or the framework for causality determination. The rationale used to select endpoints deemed to be "causal" or "likely causal" is an essential first step in the process for establishing which specific health endpoints will be carried forward for cost benefit analysis. The rule should be revised to provide the specific rationale for endpoint selection. Providing more specific detail will be critical given that some toxicity studies may be considered or evaluated differently with regard to causality determination versus establishing concentration-response functions.

2.3.2 Clarifying the scientific relevancy and applicability of Section 83.3(a)(9) requirements

Section 83.3(a)(9) of the Proposed Rule contains requirements for selecting and quantifying health endpoints in the BCA. This section should be revised to provide the rationale for some of the criteria included, the scientific relevancy of the requirements for informing the regulatory decision, and the applicability of these requirements to the data sets being evaluated. Recommendations on specific sections are included below:

- 83.3(a)(9)(ii) – This section focuses on characterizing the sources, extent (range) and magnitude of uncertainty in quantifying health hazard(s), however this information appears out of place in this section. The Agency should reorganize and place this information at the end of this section given its relevancy to section 83.3(a)10 which focuses on quantitative uncertainty analysis. It also may be useful to highlight in this section that uncertainties include both the nature of the concentration response functions as well as assumptions regarding the presence or absence of a concentration-based threshold above or below which health effects are observed (Smith, 2020).

- 83.3(a)(9)(iii)(B) – The Proposed Rule contains text which states that when selecting concentration-response relationships from the scientific literature, the Agency must select from studies where the "….pollutant analyzed in the study matches the pollutant of interest in the regulation" however it is unclear what would constitute a "match" (e.g. CAS#, chemical or physical properties). The issue of determining a "match" relies on scientific judgement that requires more objective and transparent definition. EPA should provide a clear definition of what would constitute a match.

- 83.3(a)(9)(iii)(C) – This section indicates that the "Concentration-response functions must be parameterized from scientifically robust studies." How is the Agency determining the robustness of a given study? What criteria are being used and why is "robust" an appropriate criterion to apply? Instead of including this specific criterion, the Agency should consider outlining in more general terms the systematic review process informing the selection and evaluation of the health endpoints. Implementation of criteria and methods as applied in systematic review processes would provide consistency and transparency in study selection for the purpose intended.

- 83.(a)(9)(iii)(D) – The requirements in this section state that a "study location must be appropriately matched to the analysis" and that "the study population characteristics must be sufficiently similar to those of the analysis." While both of these requirements appear reasonable, there are instances where epidemiological studies from other study locations (e.g., Canada, Europe) have been deemed relevant for U.S. regulatory decision-making because of general similarities in demographics and environmental conditions. The decision regarding whether one study location is "appropriately matched" to another is a scientific judgment that requires more objective and transparent definition. The EPA should provide a clear definition of what would constitute a study location appropriately matched to the analysis.

- 83.3(a)(9)(iv) – The section should be revised to make clear the Agency will evaluate and incorporate the results of positive, negative and null studies into its quantification of benefits, consistent with the principles of systematic review methods.

- 83.3(a)(9)(v) – This section should be revised regarding the application and relevance of the technical feasibility criterion. Specifically the Proposed Rule states that "The Agency must base decisions about the choice of the number of alternative concentration-response functions quantified for each endpoint on the extent to which it is technically feasible to quantify alternative concentration-response relationships given the available data and resources." The SAB finds that technical feasibility is an inadequate criterion and other factors should be considered. There are publications and guidance documents that provide insight into other criteria that could also be considered in order to determine the choice and number of alternative concentration-response functions that can be quantified for each endpoint (Environmental Protection Agency, 2012; Meek et al., 2014; Fedak et al., 2015). Notably, Section 83.3(a)(9)(vii)(A) of the Proposed Rule indicates that "plausible alternatives" should be considered, and this suggests that other elements beyond technical feasibility should inform the decision regarding quantification. Additionally, the Agency's current efforts to develop Consolidated Human Toxicity Assessment Guidelines may provide a more useful description of elements that can inform decision-making for dose-response analysis.

- 83.3 (a)(9)(vi) – This section states that "The Agency must select and clearly identify concentration-response functions with the strongest scientific evidence, as well as evidence necessary to demonstrate the sensitivity of the choice of the concentration-response function on the magnitude and the uncertainty associated with air pollution-attributable effects." However, the Agency provides no specific criteria regarding what constitutes the "strongest evidence;" the intent should be clearly defined in the rule and the rule should provide a definition for what is meant by "strongest evidence."

- 83.3(a)(9)(vii) – This section provides some specific information regarding what the Agency must characterize (e.g., variability, sensitivities, uncertainties) associated with the concentration-response function. However, there appears to be considerable overlap with other sections of the Proposed Rule that need to be reconciled, revised or eliminated. Some specific comments on the requirements in this section of the Proposed Rule are included below:

    - <u>The requirement to characterize the variability in the concentration-response functions across studies and models, including plausible alternatives.</u> – If different studies of the same phenomenon have used different concentration-response functions, this fact should be noted and some assessment made of how to develop a concentration-response function for the BCA (in other words, EPA should not simply use whichever concentration-response function is most convenient, or what comes closest to some preconceived desirable result). However, it should also be recognized that different studies use different study populations and statistical methods and these do not all have equal weight. Also, even for a single study, some assessment of variability could be made (for example, through standard errors or posterior distributions for the assessed concentration-response function).

    - <u>The requirement to characterize the assumptions, defaults, and uncertainties, their rationale, and their influence on the resulting estimates</u>. - It is always appropriate

to require that the assumptions, defaults, uncertainties, rationale and influence on the resulting estimates be characterized. This could be viewed as part of the general requirement for transparency in EPA decision making.

- The requirement to characterize the extent to which scientific literature suggests that the nature of the effect may vary across demographic or health characteristics. - In cases where scientific literature has considered different demographic or health characteristics, this fact should be noted and appropriately weighted in the BCA. However, it should be noted that not all scientific studies include a formal evaluation of these issues.

- The requirement to characterize the potential variability of the concentration-response function over the range in concentrations of interest for the given policy. – It is unclear how this differs from the requirement to "characterize the variability in the concentration-response functions." The Agency should consider combining the two requirements into one. This requirement may be hinting at issues such as whether to adopt a linear or non-linear model (for the concentration response function or some transformation of it, such as a logarithm) and whether to consider the possible existence of a threshold, but these are issues of scientific evidence that are difficult to encode in a precise set of rules.

- The requirement to characterize the influence of potential confounders on the reported risk coefficient. – While most epidemiological studies consider the effect of known potential confounders, there is ample room for disagreement over which confounders are appropriate, or how to evaluate an actual confounding effect (discovery of a confounding effect may raise doubts about, but need not refute, the claim of a causal effect). The language included in the Proposed Rule is vague and would be difficult to implement. EPA should transparently and objectively define the process for characterizing the influence of potential confounders, keeping mode of action in mind.

- The requirement to characterize the likelihood that the parameters of the concentration-response differ based on geographic location. – This is a good idea in principle but many epidemiological studies do not explicitly provide information that would inform this requirement and as such, the requirement may result in the exclusion of well conducted and relevant studies.

- The requirement to characterize the attributes that affect the suitability of the study or model for informing a risk assessment, including the age of the air quality data, and the generalizability of the study population. – Section 83.3(a)(9)(vii) and section 83.3(a)(9)(iii) of the Proposed Rule both discuss some study attributes that need to be considered. In those instances, the rule would benefit if the Agency clearly characterized the attributes that affect the suitability of the study or model for informing a hazard assessment and the quantification of benefits. Notably, in Section 83.3(a)(9)(vii) it is unclear what the Agency means by "age of the air quality data" or what criteria would be used to determine the relevance of a study for decision-making.

While the SAB has offered specific recommendations on the sections noted above, the Agency should consider replacing all the specific criteria in sections 83.3(a)(9)(iii) and 83.3(a)(9)(vii) with an overall framework outline of the systematic review principles it would follow for the evaluation of human health hazard data for the purposes of concentration-response selection and quantification of benefits. This overall discussion of systematic review approaches could, for example, include requirements that studies used be subject to external peer review, including a critical review of the reliability of both hazard endpoints and exposure metrics reported, account for potential confounders/co-exposures on study findings, and ensure the relevance of study attributes in supporting subsequent benefit cost analysis calculations (e.g., representative location and population characteristics in epidemiology studies).

2.3.3 Consistency and incorporation of best available and relevant systematic review approaches

As the Agency is considering best practices and approaches for the selection and evaluation of health endpoints for use in the benefit cost analysis, it must ensure consistency with current EPA approaches and recommendations of the scientific community. Section 83.3.(a)(9) provides no information regarding how current Agency practices and advice it has received from scientific review boards on data identification, evaluation and integration are being applied to the BCA. For example, the Proposed Rule provides no discussion of ongoing EPA efforts that have been supported by the Science Advisory Board, or the National Academy of Sciences, Engineering and Medicine related to the use of systematic review. The Proposed Rule also does not appear to align with the Agency's plans to develop Consolidated Human Toxicity Assessment Guidelines. The rule should be revised to include a discussion regarding how the Agency will ensure that relevant NASEM and SAB advice on systematic review as well as EPA's Consolidated Human Toxicity Assessment Guidelines will be evaluated and incorporated. Additionally, the Proposed Rule provides no discussion regarding whether relevant peer reviewed publications (Simon et al., 2016; Suter et al., 2017; Wikoff et al, 2018; Wikoff, et al., 2019) which describe how to assess uncertainty, variability and data quality evaluation in systematic review for the derivation of toxicity values were evaluated to inform the Proposed Rule. The Agency is encouraged to review and incorporate by reference or specific language relevant best practices.

2.3.4 Applicability of proposed requirements for various air pollutants

As currently written, section 83.3(a)(9) of the Proposed Rule does not provide sufficient clarity regarding the types of air pollutant regulations to which these rule requirements would apply. Specifically, the SAB recommends that this section be revised to provide clear direction regarding whether it is the Agency's intent that these scientific requirements broadly apply across all air pollutants for which EPA may develop significant regulation. The Agency should also consider providing the specific sections of the Clean Air Act to which these proposed requirements for quantifying health endpoints would apply (e.g., criteria pollutants regulated with National Ambient Air Quality Standards, hazardous air pollutants).

2.3.5 Findings and Recommendations on the Selection of Health Endpoints

- The SAB finds many of the requirements associated with the selection of health endpoints in the Proposed Rule to be vague and lacking sufficient detail that could impact effective implementation in the BCA.

- The SAB recommends the Proposed Rule be revised to clearly include the types of air pollutant regulations covered under the rule.

- The Proposed Rule should be revised to clearly provide the specific scientific rationale for endpoint selection, and transparently define specific terms used in the requirements, or the Agency should replace all of the specific criteria on the selection of health endpoints with an overall framework that relies on systematic review principles it would follow for the evaluation of human health hazard data, selection of concentration-response functions and quantification of benefits.

- The Proposed Rule should be revised to include a discussion of how the Agency will ensure that relevant advice from NASEM and the SAB on systematic review as well as EPA's Consolidated Human Toxicity Assessment Guidelines will be evaluated and incorporated.

2.4 Characterizing Uncertainty

Section 83.3(a)(10) of the Proposed Rule establishes requirements for characterizing uncertainties underlying the estimation of both benefits and costs. In this section we discuss several places where the Proposed Rule or its preamble depart from best practices and provide recommendations for improvement.

2.4.1 The Purposes of Uncertainty Analysis

Uncertainty analysis is a critical and long-standing part of benefit-cost analysis (BCA). Best practices for carrying it out are discussed in detail in both EPA's *Guidelines for Preparing Economic Analyses* and in OMB's Circular A-4.

Uncertainty analysis serves several important purposes when applied in the evaluation of proposed air rules. First, it allows analysts to determine the robustness of a BCA's results by systematically evaluating the range of possible outcomes and their likelihoods. A careful uncertainty analysis will indicate whether the BCA is relatively precise, with a narrow range of possible outcomes, or less precise, with a broad range of outcomes and potentially much larger or smaller net benefits than expected. The range of outcomes, in turn, will indicate whether the overall finding of the BCA—that is, whether the rule produces positive or negative net benefits—is robust to plausible variations in the BCA's assumptions. Providing this information to policy makers and the public is an important part of transparency in rule-making. The preamble to the Proposed Rule focuses on this aspect of uncertainty analysis.

However, a second purpose of uncertainty analysis, which is not discussed in the rule's preamble, is to guide future scientific research beyond the immediate analysis of the rule. Specifically, the analysis will indicate which underlying uncertainties contribute most to the uncertainty in overall net benefits. As discussed in both Circular A-4 and EPA's *Guidelines*, when the level of uncertainty is large, a formal value of information analysis could be applied to determine where additional scientific research would be most valuable. It could even be used to determine whether a decision should be deferred until better information can be obtained. In some cases, the additional research will take the form of new studies and data collection; in other cases, it may involve refining the existing analysis by eliminating poor studies

that are biased, are missing confounders, use poor statistical analysis, or have overstated results, and then finding improved ways to combine what is left.

A third purpose of the analysis, which is only tangentially discussed in the rule and its preamble, is to help policy makers and the public understand possible outcomes that may be far from the expected value of the rule. In particular, in contexts involving low-probability risks of catastrophic losses, policy makers and members of the public may wish to consider policies that reduce the likelihood of severe losses even though doing so may mean accepting a lower expected payoff. Moreover, understanding the range of possible outcomes can provide useful information even in the absence of catastrophic losses if the distribution of benefits is skewed. For example, the analysis could indicate that a rule has relatively little downside risk (a relatively narrow range of outcomes worse than its expected value) and relatively large upside risk (a relatively large range of potentially better outcomes), or vice versa. Characterizing the range of outcomes is critical: BCA is a tool to help policy makers and the public understand the possible consequences of policies, not a decision rule dictating that policy choices should be made solely on the basis of expected value.

2.4.2 Alignment of the Proposed Rule with Best Practices

Although uncertainty analysis is a key part of a BCA, the Proposed Rule departs from best practices in two respects.

First, both Circular A-4 and EPA's *Guidelines* recommend that the scope and extent of an uncertainty analysis be appropriate for the policy context. The Proposed Rule is insufficiently clear on this point. As written, it seems to suggest that EPA rigidly follow a prescribed set of steps that could be overly onerous or have little value for some rules.

In some cases, the rule could lead to EPA devoting resources to the uncertainty analysis that would be better spent on refining the underlying science. Even the most rigorous uncertainty analysis will be unable to correct errors resulting from the inclusion of poor science in a BCA. Identifying and removing such studies is likely to have a greater impact on the quality of a BCA than uncertainty analysis. EPA should address this issue by revising the rule to indicate explicitly that analysts have some discretion in designing and carrying out the analysis. In particular, the Proposed Rule explicitly expands the domain of policies subject to BCA beyond those previous considered "significant" under Section 3(f) of Executive Order (EO) 12866 (Clinton, 1993). The existing class of significant rules already varies enormously in importance to the environment, the economy, and overall public wellbeing. Sometimes under EO 12866 a rule is declared significant simply because it includes a novel legal interpretation rather than important environmental or economic impacts. Under the new interpretation, the range of policies to be evaluated will be even broader. As a result, the agency should reconsider whether requiring the same degree of complexity in the uncertainty analysis of every policy is appropriate.

Moreover, as written the Proposed Rule recommends formal probabilistic uncertainty analysis for all policies deemed significant under the rule's expanded definition of the term. However, both Circular A-4 and EPA's *Guidelines* only recommend probabilistic analysis for economically significant rules with impacts larger than $1 billion per year: both agencies regard a deterministic sensitivity analysis to be adequate for rules with lower impacts. The Agency should explain why the broader application of probabilistic analysis has been judged appropriate or, alternatively, it should consider using the $1

billion threshold to determine when some of the more intensive methods of uncertainty analysis, such as probabilistic analysis, are required.

The rule's second departure from best practices is that it may lead analysts to focus too heavily on the expected value of a policy and not give adequate attention to other values in the range of likely outcomes. As noted above, a BCA should provide policy makers and the public with broader information: the expected value of a policy is rarely the only criterion for a decision. In fact, BCA is often most valuable when uncovering marginal impacts of policy options such as inclusion of a subsector of industry or adjustments in the policy's timing. Moreover, focusing heavily on expected value will be particularly inappropriate when there are thought to be significant unquantified benefits or costs. This could be addressed by revising Section 83.3(a)(10)(vi) to increase its emphasis on outcomes beyond the expected value, and to note the need for acknowledging unquantified benefits or costs, where appropriate.

2.4.3 Recommendations on Uncertainty Analysis

- The preamble should be revised to discuss the broader purposes of uncertainty analysis beyond simple transparency.

- In several places the Proposed Rule should be revised to align it with best practices, which require that the analysis be appropriate for the policy context. This can largely be done by replacing the words "to the extent feasible" with "to the extent feasible and appropriate."

- The discussion in Section 83.3(a)(10)(vi) should be broadened to reflect the fact that outcomes other than the expected value may be very important for policies involving low-probability, high-consequence hazards. Also, when presenting quantitative results EPA should also clearly note when there are unquantified benefits or costs that could be significant.

- The discussion should note that uncertainty analysis will not correct errors resulting from the inclusion of poor science, which arguably has a greater impact on policy choices.

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