

TO: Clean Air Scientific Advisory Committee
United States Environmental Protection Agency

SUMMARY OF TESTIMONY TO BE PROVIDED TO THE CLEAN AIR
SCIENTIFIC ADVISORY COMMITTEE DURING THE CASAC MEETING
ON THE DRAFT PARTICULATE MATTER ISA HELD DECEMBER 12-13,
2018

DECEMBER 5, 2018

NCASI agrees with the mission of the Environmental Protection Agency (EPA) under the Clean Air Act to protect public health by setting National Ambient Air Quality Standards (NAAQS). However, this policy should be supported by the best available science, integrated within a reliable systematic review framework that produces an accurate characterization of the relationship between criteria pollutants such as particulate matter and potential health effects.

Several institutions that support science-based policy development have pursued the adoption of increasingly rigorous systematic review methodologies, including the National Toxicology Program (NTP) under the Toxic Substances Control Act (TSCA), the National Academies of Sciences (NAS), and EPA's Integrated Risk Information System (IRIS) program. The effort undertaken by these institutions to adopt more rigorous systematic review procedures is done in order to more accurately rank, weight, and evaluate quality of individual studies within a framework to more reliably draw conclusions related to exposure/disease relationships.

A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question. It uses explicit, systematic methods that are selected with a view to minimizing bias, thus providing more reliable findings from which conclusions can be drawn and decisions made. The key characteristics of a systematic review are:

- a clearly stated set of objectives with pre-defined eligibility criteria for studies;
- an explicit, reproducible methodology;
- a systematic search that attempts to identify all studies that would meet the eligibility criteria;
- an assessment of the validity of the findings of the included studies, for example through the assessment of risk of bias; and
- a systematic presentation, and synthesis, of the characteristics and findings of the included studies.

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The EPA NAAQS Framework for Causal Determination lacks most critical features of systematic review, leaving the Draft ISA vulnerable to introducing to risk of bias and impairing the reliability of its conclusions.

The research questions in the Draft ISA are have not been developed specifically enough to properly inform the downstream review criteria of study selection and study quality. Due to imprecise framing of research questions, there is no assurance that the appropriate literature in terms of both relevance and quality have been selected to address these questions.

The literature selection process in the Draft ISA lacks critical features of systematic review. The lack of methodological detail present in the ISA impairs the reproducibility of the science assessment, impairs the transparency of the science assessment, and does not assure that studies of appropriate relevance and quality are used to address charged research questions. As a result, the reliability of the conclusions presented in the Draft ISA are impaired.

The issue of confounding is not adequately evaluated in the Draft ISA in terms of the existence of both residual confounding in studies and unmeasured confounding in studies. Without a systematic approach to evaluate and appropriately include or disqualify studies based on the issue of confounding, a substantial risk of bias exists in the ISA review process that impairs the reliability the conclusions presented. This is of particular importance when considering the small effect sizes that are presented in the ISA findings.

The Draft ISA does not have a systematic approach to evaluate the impact of model specifications and underlying model assumptions on study quality. This is of particular importance for models that rely on an underlying assumption of linearity, as a violation of this assumption reduces the accuracy of low exposure risk estimates and may artificially prevent the detection of a toxicity threshold. Without a pre-defined systematic approach to evaluate the impact of model and statistical method assumptions on study quality, the reliability of the conclusions presented in the Draft ISA are impaired.

Publication bias is acknowledged as likely to be present in the literature reviewed in the Draft ISA and data is presented that demonstrates its impact. However, no systematic approach exists in the Draft ISA to evaluate and adjust for the impact of publication bias in the review. The reliability of the conclusions presented in the Draft ISA are impaired by not accounting for the presence of publication bias, particularly when tools exist to address this issue.

The Draft ISA lacks a pre-defined method to integrate lines of evidence such that both strength of evidence and weight of evidence are evaluated to accurately characterize preponderance of findings of high-quality studies. In particular, there is a deficiency in the prescribed integration of Mode of Action studies and the reconciliation of divergences in the concentration-response between toxicological studies and epidemiological studies. The lack of a systematic approach to integrate these lines of evidence impairs the reliability of the conclusions presented in the Draft ISA.

Systematic reviews rely on pre-defined, objective criteria to reach judgements of causality. The lack of a systematic approach in the Draft ISA has led to a deficiency of rigorous, objective criteria (or even well-defined criteria) to reach conclusions of causality. There is a substantial reliance on subject matter expertise in the interpretation of lines of evidence. As a result of not employing a systematic approach to reach conclusions regarding causality, the reliability of the conclusions presented in the ISA are impaired.

Due to the lack of a systematic approach in the Draft ISA and the heavy reliance on subject matter experts for the interpretation of study quality, the conclusions of the Draft ISA have been made vulnerable to risk of bias from the potential mis-application of the precautionary principle and confirmation bias. As a result, the

reliability of the conclusions presented in the Draft ISA are impaired.

As a result of the lack of a systematic approach, the process used in the development of the current ISA for particulate matter introduces uncertainty and bias at every stage of the review process and is unable to adequately characterize the relationship between particulate matter and health outcomes. The ISA should be conducted with a systematic approach to be considered the 'best science' on this issue. In the absence of an ISA developed using a systematic review approach, the various limitations from not doing so should be stated explicitly in the ISA so that those who would use this document as a resource for policy decision making are aware of the profound amount of uncertainty that is associated with the conclusions presented.

While we very much appreciate the time provided to give testimony on these issues, it is not enough time to adequately present the details of our technical evaluation. Please refer to our detailed written comments submitted in conjunction with this testimony for a more in depth look at the issues discussed here.

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