

Sheppard Oral Comments October 22, 2019

Members of the Clean Air Scientific Advisory Committee:

Thank you for the opportunity to speak to you today about EPA's most recent Policy Assessment for particulate matter. As a member of the Independent Particulate Matter Review Panel, I wish to affirm that my professional reputation and integrity stand behind our consensus comments, released to the public today. I also want to speak to the power of a deeply engaged scientific conversation with a sufficiently large group of experts about the document you are charged with reviewing. Twenty of us met for two days and discussed every part of the Policy Assessment in depth. I found that our collective, thoughtful review enabled me to better understand many important aspects of the PA and the recommendations put forth by EPA. While EPA crafted a strong and well-reasoned PA document, an undertaking even more impressive given their highly compressed schedule, our Panel highlighted aspects of the document that deserve more development and recommended that the PA be revised. Regardless, we found the PA to be credible and its judgment sound that the evidence calls into question the current standards. Furthermore, we found EPA's arguments for retaining the current standards specious and not scientifically valid.

The PA does not deserve a wholesale revamping and should not discount the studies considered, a perspective I have gleaned from the preliminary comments of some CASAC members. In particular, I wish to talk about the scientific evidence and the causal conclusions drawn from it.

First, in addressing Dr. Packham's concerns about the use of the words "science" and "scientific" in the document, when EPA uses these terms, it is referring to the vast body of scientific evidence that it has distilled from published peer-reviewed research in the scientific literature. EPA only considers scientific evidence that is published in the peer-reviewed literature. This pertains to all disciplines relevant to the ISA review, including papers that address air quality, exposure science, epidemiology, toxicology, and controlled human exposure studies. It does not include the risk assessment analyses that were also covered in the PA. (Note: A risk assessment is typically covered in a separate Risk and Exposure Assessment document. This was planned to be part of this PM review process but scrapped as a separate document with the wholesale revision of the process put forth by the EPA Administrator in the fall of 2018. I sympathize with your challenge in digesting this review when multiple steps of the process have been condensed into one.)

Second, both Dr. Lange and Dr. Cox argue that EPA needs to incorporate relatively recently developed statistical methods for causal inference in this review. EPA relies on a distillation of evidence from the published literature for its scientific review. They apply a weight of evidence causal determination framework that considers all the evidence in total. This framework is an

appropriate tool for drawing causal conclusions that incorporates information from multiple disciplines and types of studies; it has been well-vetted over more than a decade by many previous CASAC reviews. This framework has also been used by many other regulatory bodies, and is consistent with frameworks reviewed by the Institute of Medicine. Most, but far from all the weight of evidence for PM_{2.5} health effects comes from epidemiologic studies. The epidemiologic evidence is vast, particularly in terms of the geographic domain and number of subjects included; it provides an overall consistent scientific basis, supported by coherence with controlled human and toxicological studies, for finding that the current primary PM_{2.5} standards are not protective of public health. All these studies have been conducted and analyzed using accepted scientific methods. It is beyond the scope of EPA's mandate for EPA to reanalyze existing published peer-reviewed studies using causal inference methods as a condition of a study being considered in EPA's weight of evidence review. While it may be possible for EPA to integrate published papers that apply emerging causal inference tools in future reviews, as I discuss with Drs. Carone and Dominici in our in press commentary in *Epidemiology*, these emerging tools still require considerable development before they can be implemented in air pollution epidemiology studies. (Carone et al in press).

Furthermore, Dr. Lange argues (preliminary comments p 32) that in determining a hazard (which is predominantly done in the ISA, and then discussed in the PA) based on a controlled human exposure study, that it is necessary to consider exposure levels simultaneously. In fact, requiring a hazard assessment to be conducted at typical exposure levels will often require enormous sample sizes and thus will mandate unaffordable human exposure or animal toxicological studies. The PA does take into account exposure for studies in its review by considering mean exposures (as well as estimating pseudo-design values for epidemiologic studies). It fails to consider how the human exposure study levels relate to a 24-hour standard given these controlled human exposures typically last only 2 hours. By revisiting this omission, the EPA may learn that the controlled human exposure studies may have much more meaningful exposures at the level of the 24-hour standard.

The scientific evidence alone is sufficient for drawing the causal conclusions. It is not necessary to consider the risk assessment in considering whether the current standards are adequate. Notably, to dispute EPA's preliminary conclusion that the current standards are not sufficiently protective, it is necessary to conclude all of the following:

- That the vast body of epidemiologic evidence is not informative
- That the body of experimental evidence from animal toxicology and controlled human exposure studies, along with understanding of biological pathways and mechanisms for action, is not informative
- That further decreases in ambient PM_{2.5} concentrations will not lead to public health benefits

- That uncertainties in the risk assessment are so large as to render it uninformative

I find it implausible for all of these requirements to be met.

Thank you for your attention today.

Reference:

Carone M, Dominici F, Sheppard L. In pursuit of evidence in air pollution epidemiology: The role of causally driven data science. *Epidemiology*, 2019, in press. NIHMSID 1535952. Available online August 12, 2019.
https://journals.lww.com/epidem/Citation/publishahead/In_Pursuit_of_Evidence_in_Air_Pollution.98513.aspx