



May 13, 2016

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Re: Response to US EPA's Charge Questions on the Draft Integrated Review Plan (IRP) for the National Ambient Air Quality Standards (NAAQS) for Particulate Matter (PM)

Dear Dr. Diez Roux:

I appreciate the opportunity to provide feedback to the Clean Air Science Advisory Committee (CASAC) in advance of its review of the Draft Integrated Review Plan (IRP) for the National Ambient Air Quality Standards (NAAQS) for Particulate Matter (PM) (US EPA, 2016a). These comments were prepared with funding by the American Petroleum Institute.

The body of research evidence to be reviewed is tremendous in its volume and complexity, and US EPA has presented a comprehensive and clear plan for the upcoming review. I have identified only a few aspects of the IRP that could be clarified and/or strengthened. Attached, I present my suggestions in response to the charge questions US EPA issued to CASAC (US EPA, 2016b).

Thank you for considering my review of the IRP, and I look forward to any questions you may have.

Sincerely,

GRADIENT

/s/

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Principal

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References

US EPA. 2016a. "Draft Integrated Review Plan for the National Ambient Air Quality Standards for Particulate Matter." National Center for Environmental Assessment (NCEA), Office of Air Quality Planning and Standards, 150p., April.

US EPA. 2016b. Memorandum to A. Yeow (US EPA, Clean Air Scientific Advisory Committee (CASAC)) re: CASAC review of the "Draft Integrated Review Plan for the National Ambient Air Quality Standards for Particulate Matter." Office of Air Quality Planning and Standards, 4p., April 14.

Response to US EPA's Charge Questions on the Draft Integrated Review Plan (IRP) for the National Ambient Air Quality Standards (NAAQS) for Particulate Matter (PM)

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1 Overall Organization and Clarity

To what extent does the Panel find that the draft IRP is clearly organized and that it appropriately communicates the plan for the current review of the PM NAAQS and the key scientific and policy issues that will guide the review?

The IRP (US EPA, 2016a) is clearly organized and, for the most part, highly effective in communicating the plan. As described in the relevant sections below, CASAC might consider requesting some additional detail in the next draft of the IRP, especially in regards to the planned approaches for literature selection, individual study quality assessment, and interpretation of epidemiology data in light of potential exposure measurement errors.

2 Chapter 2 (Key Policy-Relevant Issues in the Current Review)

To what extent does the Panel find that Chapter 2 clearly articulates the decisions made in the last review of the primary (Sections 2.1.1, 2.1.2) and secondary (Sections 2.2.1, 2.2.2) PM standards, and the rationales supporting those decisions?

These sections to be clearly articulated. US EPA has summarized a complex set of issues and decisions very well.

To what extent does the Panel find that the policy-relevant questions presented in Sections 2.1.3 (primary) and 2.2.3 (secondary) appropriately characterize the key scientific and policy issues for consideration in the current review? Are there additional issues that should be considered?

The policy-relevant questions presented appropriately characterize many of the key issues that should be considered in this review. CASAC should consider recommending that US EPA include additional questions to address the following issues:

- Expanding upon the question, "To what extent have important uncertainties in the evidence from the last review been addressed, and have new uncertainties emerged?" US EPA could further ask, "To what extent, if at all, does evolving knowledge of uncertainties in various realms of research (e.g., emerging theories for mechanisms of postulated effects, or exposure measurement error) affect EPA's interpretation of the evidence evaluated in the last review?"
- Regarding the set of questions beginning, "What does the evidence indicate with regard to confidence in the occurrence of health effects...", the questions could be re-written to include

emphasis on evidence derived from experimental studies, such as controlled exposure, animal, and mechanistic studies, in addition to observational studies. Specifically, the first sub-question regarding low-dose health effects and the shape of the concentration response function (CRF) only mentions epidemiology findings; but controlled human exposure, animal experiments, and mechanistic research should be considered as well. Further, this set of questions could include a question addressing coherence in findings across realms; *e.g.*, "To what extent are findings across various realms coherent, including with respect to dose-response relationships at low does?"

- Regarding the proposed question addressing co-pollutant confounding, US EPA should add a question to guide a review of emerging methods for evaluating confounding by co-pollutants as alternatives to multivariate regression, the most common approach at the time of the last review. This may include a re-evaluation of conclusions regarding co-pollutant confounding in US EPA's last review, which was driven primarily by results of multi-pollutant regression modeling.
- As discussed in response to Chapter 3 charge questions, below, CASAC should consider suggesting an additional key policy-relevant question focused on the evaluation of exposure measurement error and its implications for the interpretation of observational epidemiology studies.
- US EPA should include one or more policy-relevant questions focused on mode of action (MoA) evidence. For example: Do the mechanistic studies show clinically relevant changes (*e.g.*, biomarkers that overwhelm homeostatic mechanisms) relevant to the apical endpoint of interest? Are MoA studies consistent, coherent, and of sufficient methodological quality for use in making causal conclusions?

3 Chapter 3 (Science Assessment)

To what extent does Chapter 3 clearly and adequately describe the scope, specific issues to be considered, and organization of the ISA?

- Overall, the descriptions were well-written. A minor issue is that Sections 3.1 and 3.4 seem to be somewhat redundant. An improved approach to Chapter 3 could include making Section 3.1 very brief and shifting much of the important content in 3.1 to 3.4, to produce one list of specific issues to be addressed in the ISA in Section 3.4.
- It would be helpful to have a simpler, clearer presentation of the proposed ISA organization, such as a draft outline of the ISA, which could be included in an appendix.

What are the panel's views on the overall scope of the ISA? Does the planned scope ensure that the EPA will capture the scientific literature most pertinent to the ISA's focus, which is answering the question, "Is there an independent effect of PM on health and welfare at relevant ambient concentrations?"

- CASAC should consider requesting more clarity in US EPA's plans for conducting literature searches and, especially, for selecting studies to be included in the ISA (both older and new studies since the last review cycle) (Section 3.3.2). Given the very large number of studies within each realm that will be identified in initial literature searches, it is critical that US EPA be as specific as possible, *a priori*, in describing inclusion/exclusion criteria. Doing so will increase the objectivity and transparency of US EPA's selection of evidence to include in the ISA and reduce the potential for bias.
- Similarly, CASAC should request additional details in US EPA's plans to evaluate individual study quality, as well as in US EPA's plans to utilize the results of study quality assessments in

the evidence integration (Section 3.3.3). US EPA presented a thorough and science-based set of study quality criteria in the 2015 NO_x ISA, and this as an important step forward in increasing objectivity and transparency. CASAC should make recommendations for US EPA to describe its intended approach for applying these criteria in the PM ISA in a way that is unbiased and transparent. Applications of the study quality criteria may include identifying "key references," which were defined by US EPA in the NO_x ISA as high-quality studies carrying the most weight in the causal determinations. US EPA did not describe the application of the criteria in distinguishing key, high-quality studies for the NO_x ISA, however; CASAC should guide US EPA to develop a plan for identifying high-quality studies in a transparent manner in the PM ISA. Although any set of study quality criteria, no matter how carefully defined, are to some extent subjective and uncertain; therefore, as discussed by the NO_x CASAC committee (US EPA, 2015), the criteria should not be misapplied as a strict "checklist."

- In the IRP, the causal framework applied in NAAQS evaluations is discussed in Section 3.4.3. CASAC should reevaluate US EPA's "suggestive" category. At present, almost any large body of evidence could be placed into this category, since US EPA notes that a large database of "varying quality" could be judged to be "generally supportive," yet it provides no direction for determining how a body of evidence that is "not entirely consistent" would qualify as "suggestive" as opposed to "inadequate."
- US EPA has done an excellent job of summarizing the key atmospheric science questions that should be answered in the ISA in the section on atmospheric chemistry (Section 3.4.4). To build on this foundation, CASAC should encourage US EPA to evaluate whether important findings related to atmospheric science are robust to the different experimental approaches utilized between studies. For example, US EPA might ask whether different atmospheric chemistry models produce varying information on PM source attribution, or whether there are meaningful variations in results of studies reporting particle size difference when the results are based on modeling *versus* direct observation of differences.
- US EPA has comprehensively and articulately addressed many issues and challenges related to estimating human exposure. CASAC should encourage US EPA to detail its plan to coherently apply these findings in Section 3.4.8 of the IRP, which describes the assessment of health effects. In CASAC's feedback on the recent SO_x ISA (US EPA, 2016b), CASAC panelists expressed concern that the review of evidence regarding human exposure was not coherently extended to a discussion of exposure measurement error and potential effects on epidemiology results, including bias towards or away from the null. At this stage of the PM review, US EPA has the opportunity to develop a detailed and transparent approach for reviewing aspects of human exposure to PM as well as specific plans for interpreting epidemiology data in light of exposure measurement error (to the degree possible for published studies).
- Section on MoA (Section 3.4.7): US EPA has outlined several important questions with regard to PM modes of action, including how particle characteristics and interspecies differences affect biological response. However, this section could be even stronger with additional discussion of US EPA's plans to integrate MoA evidence with other realms. For example, US EPA should assess whether the mechanistic studies report clinically relevant changes (*e.g.*, biomarkers that overwhelm homeostatic mechanisms) relevant to the apical endpoint of interest. US EPA could also explicitly indicate that it will evaluate whether MoA studies are consistent, coherent, and of sufficient methodological quality for use in making causal conclusions.
- The list of policy-relevant questions in the section on health effects (Section 3.4.8) is thorough and well-written. CASAC should consider suggesting a couple minor improvements, such as including questions addressing coherence between results from various realms of research as well

as questions to guide US EPA in evaluations of exposure measurement error and its effects on the interpretation of epidemiology data.

4 Chapter 4 (Health Risk and Exposure Assessment)

To what extent does Chapter 4 clearly and adequately describe the scope and specific issues, including the identification of the most important uncertainties, to be considered in developing the HREA Planning Document for this review?

US EPA indicated it would consider both an epidemiology-based risk assessment and an exposure assessment, as is currently described in the draft IRP. US EPA summarized many key points in the IRP, and these will likely be expanded upon in the HREA Planning Document after the ISA has been conducted. CASAC should encourage US EPA to also consider the following comments.

With regard to the epidemiology-based risk assessment:

- In addition to listing criteria that will be used to identify the urban study areas in the HREA Planning Document, it would be useful to include more details on how they will be applied, including an approach to prioritizing competing criteria. In addition, it would also be helpful for US EPA to specify the method it will use to determine whether the selected study areas are representative of other urban areas across the country.
- As part of assessing PM concentration adjustment approaches (e.g., proportional roll-back), it would be useful to consider methods by which the uncertainty in these roll-back approaches can be quantified, and whether these roll-back approaches can be used to evaluate PM compositional differences under alternative standards.

With regard to the exposure assessment:

- As with the epidemiology-based risk assessment, CASAC should encourage US EPA to provide a detailed explanation of the urban study area selection method in the HREA Planning Document (see above).
- US EPA provided an excellent summary of many of the uncertainties inherent to the APEX model. CASAC should encourage US EPA to consider the following factors influencing uncertainty in the APEX model: the number of simulated persons used per model run, the model seed value used (or use of a random model seed), and influences of indoor sources of PM.
- CASAC should encourage US EPA to describe the method that will be used to assess whether APEX evaluations can be conducted for size fractions beyond PM_{2.5} (e.g., for PM_{10-2.5} or ultrafine particles).

5 Chapter 5 (Welfare Risk and Exposure Assessment)

To what extent does Chapter 5 clearly and adequately describe the scope and specific issues, including the identification of the most important uncertainties, to be considered in developing the WREA Planning Document for this review?

In the draft IRP, US EPA mentions that it will re-evaluate the results and validity of the visibility preference studies US EPA utilized in the previous review to inform the welfare assessment. These studies warrant an assessment of study quality and potential biases if they will carry weight in the updated welfare risk assessment.

References

US EPA. 2015. Letter to G. McCarthy (US EPA) re: CASAC Review of the EPA's "Integrated Science Assessment for Oxides of Nitrogen – Health Criteria (Second External Review Draft – January 2015)" (Draft). Clean Air Scientific Advisory Committee (CASAC), 28p., July 16.

US EPA. 2016a. "Draft Integrated Review Plan for the National Ambient Air Quality Standards for Particulate Matter." National Center for Environmental Assessment (NCEA), Office of Air Quality Planning and Standards, 150p., April.

US EPA. 2016b. Letter to G. McCarthy (US EPA) re: CASAC Review of the EPA's "Integrated Science Assessment for Sulfur Oxides – Health Criteria (External Review Draft – November 2015)" (Draft). Clean Air Scientific Advisory Committee (CASAC), EPA-CASAC-16-XXX, 115p., March 10.