Preliminary Comments from Members of the

Independent Particulate Matter Review Panel

on

EPA's Policy Assessment for Review of the National Ambient Air Quality Standards for Particulate Matter (External Review Draft – September 2019)

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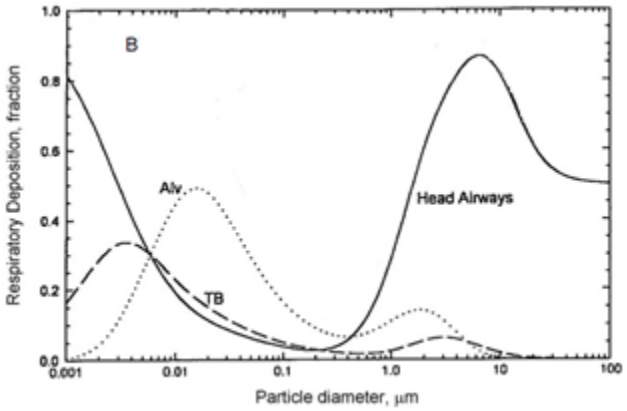
EPA-1. Chapter 1 – Introduction: To what extent does the CASAC find that the information in Chapter 1 is clearly presented and that it provides useful context for the review?

Chapter 1 provides a useful starting point.

The depiction of particle sizes in Figure 2-1 does not provide information with regard to why particle size might be important. A discussion of the role of particle size on lung deposition would be appropriate and would provide context for the later discussion of health effects of PM as a function of size. A diagram would be useful and could be discussed later as one talks about the differences between coarse and fine PM.



EPA-2. Chapter 2 – PM Air Quality: To what extent does the CASAC find that the information in Chapter 2 is clearly presented and that it provides useful context for the review?

SCQ-2.1 What are the panel's views regarding whether the draft PA accurately reflects and communicates the air quality related information most relevant to its subsequent evidence-based assessment of the health and welfare effects studies, including uncertainties, as well as the development of the risk assessment for current and alternative standards? In particular, do the following sections accurately reflect and communicate current scientific understanding, including uncertainties, for: (a) relationships between annual and daily distributions of PM; (b) the review of hybrid modelling approaches used to estimate exposure in some studies and the risk assessment; and (c) information on background levels of various PM indicators?

The discussion of the relationships between daily and annual distributions of PM would have benefitted from some integration with potential mechanisms of toxicity. Many of the disease-causing or exacerbating processes induced by PM exposures is related to formation of free radicals and the development of oxidative stress and inflammation. While in healthy individuals there are innate defenses against oxidative stress, One reason to be concerned with short term peak exposures is that normal defenses can be overwhelmed (i.e antioxidants can be consumed faster than they can be replenished) and the un-neutralized free radicals can injure tissues

and organs. In the California Bay Area there were 13 occasions for which the daily average was below the NAAQS of 35 µg/m3 but there were 1 hr peak concentrations greater than 3 times the NAAQS, ranging from 113 TO 415 µg/m3 (mean concentration = 197 ± 102). These days were distributed over various stations in the Bay area and the interval was Feb to November 2018. Thus, on days when the 24hr concentration was within the NAAQS people were exposed for at least 1 hr to PM2.5 concentrations that were equivalent to the levels used in controlled human studies, documented in Table 3-1 from the PA. Note that November 2018 was a severe fire month and there were several days above the NAAQS 24 hr standard and 1 hr concentrations exceeding 105 µg/m3, but the other months with high 1 hr peak exposures were most likely not fire-related.

Table 3-2. Summary of information from $PM_{2.5}$ controlled human exposure studies.

Study	Population	Exposure Details (average concentration; duration)	Results
Bräuner et al., 2008	Healthy adults	10.5 µg/m³ $PM_{2.5}$ (unfiltered) vs below detection (filtered); 24 h	No significant effect on markers of vascular function
Hemmingsen et al., 2015a, Hemmingsen et al., 2015b	Healthy, overweight older adults	24 µg/m³ (unfiltered) vs 3.0 µg/m³ (filtered) Copenhagen PM; 5 h	Impaired vascular function and altered heart rate variability; no significant changes in blood pressure or markers of inflammation or oxidative stress
Urch et al., 2010	Non-asthmatic and mild asthmatic adults	64 µg/m³ CAP (lower exposure); 2 h	No significant change in blood markers of inflammation or oxidative stress
Huang et al., 2012	Healthy adults	90 µg/m³ CAP; 2 h	No significant changes in heart rate variability
Devlin et al., 2003	Healthy older adults	99 µg/m³ CAP[28]; 2 h	Decreased heart rate variability
Hazucha et al., 2013	Adult current and former smokers	109 µg/m³ CAP; 2 h	No significant changes in markers of inflammation or coagulation
Ghio et al., 2000	Healthy young adults	120 µg/m³ CAP; 2 h	Increased fibrinogen (coagulation)
Ghio et al., 2003	Healthy young adults	120 µg/m³ CAP; 2 h	Increased fibrinogen; no significant effect on markers of inflammation
Urch et al., 2010	Non-asthmatic and mild asthmatic adults	140 µg/m³ CAP (higher exposure); 2 h	Increased blood inflammatory markers
Brook et al., 2009	Healthy adults	149 µg/m³ CAP; 2 h	Impaired vascular function, increased blood pressure; no significant change in markers of inflammation (compared to filtered air)
Ramanathan et al., 2016	Healthy adults	149 µg/m³ CAP; 2 h	Decreased anti-oxidant/anti-inflammatory capacity when baseline capacity was low

Sivagangabalan et al., 2011	Healthy adults	150 µg/m³ CAP; 2 h	Increase in indicator of possible arrhythmia; no significant effect on heart rate
Kusha et al., 2012	Healthy adults	154 µg/m³ CAP; 2 h	No significant effect on indicator of possible arrhythmia
Gong et al., 2003	Adults with and without asthma	174 µg/m³ CAP; 2 h	Increased heart rate; No significant effect on indicators of arrhythmia, inflammation, coagulation; inconsistent effects on blood pressure
Gong et al., 2004	Older adults with and without COPD	200 µg/m³ CAP; 2 h	Decreased heart rate variability, increase in markers of inflammation (without COPD only); inconsistent effect on arrhythmia; no significant effect on markers of blood coagulation
Liu et al., 2015	Healthy adults	238 µg/m³ CAP; 130 min	Increase in urinary markers of oxidative stress and vascular dysfunction; no significant effect on blood markers of oxidative stress, vascular function, or inflammation
Bellavia et al., 2013	Healthy adults	~242 µg/m³ CAP; 130 min	Increased blood pressure
Behbod et al., 2013	Healthy adults	~250 µg/m³ CAP; 130 min	Increase in markers of inflammation
Tong et al., 2015	Healthy older adults	253 µg/m³ CAP; 2 h	Impaired vascular function and increased blood pressure; no significant change in markers of inflammation or coagulation
Lucking et al., 2011	Healthy young men	320 µg/m³ (unfiltered) vs 7.2 µg/m³ (filtered); 1 h	Impaired vascular function and increased potential for coagulation; no significant effect on blood pressure, markers of inflammation, or arterial stiffness
Vieira et al., 2016a, Vieira et al., 2016b	Healthy adults; Heart failure patients	325 µg/m³ (unfiltered) vs 25 µg/m³ (filtered) diesel exhaust; 21-min	Increase in marker of potential impairment in heart function, impaired vascular function (heart failure patients); no significant effect on blood pressure, heart rate or heart rate variability, markers of inflammation, markers of coagulation, or arterial stiffness

EPA-3. Chapter 3 – Review of the Primary $PM_{2.5}$ Standards: What are the CASAC views on the approaches described in Chapter 3 to considering the $PM_{2.5}$ health effects evidence and the risk assessment in order to inform preliminary conclusions on the primary $PM_{2.5}$ standards? What are the CASAC views regarding the rationales supporting the preliminary conclusions on the current and potential alternative primary $PM_{2.5}$ standards?

SCQ-3.1 Does the panel find that the questions posed in this chapter appropriately reflect the important policy-relevant issues for the $PM_{2.5}$ review? Are there additional policy-relevant questions that should be addressed?

The question of the importance of short term standards is one that deserves additional consideration. In fact the human controlled exposures suggest that a shorter term (1 hr ?) acute standard might have some protective value.

Based on the discussion for 2.1, the controlled human studies, which found significant cardiovascular effects should be considered as relevant to actual exposures and taken into stronger consideration with respect evaluating the adequacy of the current NAAQS levels.

SCQ 3.3 What are the panel's views on the evidence-based approach, including: The preference for continuing the use of an annual $PM_{2.5}$ standard as the principle means of providing public health protection against the bulk of the distribution of short- and long-term $PM_{2.5}$ exposures?

The use of the annual standard to protect against short and long term exposure health effects may not be the best approach, from the standpoint of biological mechanisms. As stated earlier, many of PM's health effects are subsequent to formation and release of free radicals leading to oxidative stress and inflammation. These are hallmarks of heart diseases, lung diseases, cancer and degenerative nerve diseases. While in healthy individuals there are innate defenses against oxidative stress, short term peak exposures can overwhelm the normal immunological defenses (i.e antioxidants can be consumed faster than they can be replenished) and the un-neutralized free radicals can injure tissues and organs. This could be especially true in people with impaired immunity, people with pre-existing diseases, the very young and the elderly.

SCQ-3.5 What are the panel's views on the draft PA preliminary conclusion that, taken together, the available scientific evidence, air quality analyses, and the risk assessment can reasonably be viewed as calling into question the adequacy of the public health protection afforded by the current primary $PM_{2.5}$ standards?

The evidence and discussion consistently demonstrate that the current standards do not provide an adequate margin of safety to prevent health effects. It should be noted that while the weight of evidence for PM's effects cardiovascular disease causation is stronger than that for pulmonary disease, having an impaired pulmonary system will put significant extra load on the cardiac system and could be a contributing factor to the ultimate cause of death, i.e. cardiac-related disease.

GC-1. What scientific evidence has been developed since the last review to indicate if the current primary and/or secondary NAAQS need to be revised or if an alternative level or form of these standards is needed to protect public health and/or public welfare? Please recommend to the Administrator any new NAAQS or revisions of existing criteria and standards as may be appropriate. In providing advice, please consider a range of options for standard setting, in terms of indicators, averaging times, form, and levels for any alternative standards, along with a description of the alternative underlying interpretations of the scientific evidence and risk/exposure information that might support such alternative standards and that could be considered by the Administrator in making NAAQS decisions.

Shorter averaging times (1 hr ?) to protect against acute health effects (sudden cardiac death, acute asthma attacks)

GC-2. Do key studies, analyses, and assessments which may inform the Administrator's decision to revise the NAAQS properly address or characterize uncertainty and causality? Are there appropriate criteria to ensure transparency in the evaluation, assessment, and characterization of key scientific evidence for this review?

There are appropriate criteria that are relevant to any scientific endeavor. Thorough documentation of methods and approaches, documentation of quality control and quality assurance, rigorous, objective analysis of the data are all necessary. The studies that were discussed in the documents were evaluated and selected because they were quality science.

GC-3. Are there areas in which additional knowledge is required to appraise the adequacy and basis of existing, new, or revised NAAQS? Please describe the research efforts necessary to provide the required information.

New areas of health effects studies and new assessment methods are continuing to evolve. Evaluation and characterization of "hot spots" of high exposure, especially where those areas can be identified with impacts from local sources are needed.

GC-4. What is the relative contribution to air pollution concentrations of natural as well as anthropogenic activity? In providing advice on any recommended NAAQS levels, please discuss relative proximity to peak background levels.

Recent laboratory studies have demonstrated that natural organic vapors when combined with atmospheric photochemical processes and anthropomorphic combustion gases (NOx) form particles that are more toxic than secondary organic particles formed in the absences of the human pollutants. Some future attention to these could be warrented.

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