Secretariat:
Infinity Conference Group
(Contact: Doreen Albertson)
1035 Sterling Road
Herndon, VA 20170
703-925-0178 (Voice) 703-925-9453 (Fax)
secretariat@iseepi.org (E-Mail)
www.iseepi.org (website)

Administrator Michael S. Regan
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

November 29, 2021

Re: Docket No. EPA-HQ-ORD-2014-0859
COMMENTS: Supplement to the 2019 Integrated Science Assessment for Particulate Matter (External Review Draft, 2021)

To the Administrator:

We, the North American Chapter of the International Society for Environmental Epidemiology (ISEE), are in support of the EPA's decision to reconsider the December 2020 decision to retain the current particulate matter (PM) National Ambient Air Quality Standards (NAAQS). The current annual **primary standard** (i.e., to provide public health protection) for $PM_{2.5}$ is 12.0 micrograms per cubic meter ($\mu g/m^3$) annual mean, averaged over 3 years. The current annual secondary standard (i.e., to provide public welfare protection) for $PM_{2.5}$ is 15.0 $\mu g/m^3$ annual mean, averaged over 3 years. In our view, retaining the current standards would fail to meet EPA's mandated responsibility, which according to the Clean Air Act,[1] includes setting air quality standards that provide sufficient public health protection for all, including at-risk groups.

The goal of the EPA Administrator in selecting a primary PM standard is to "prevent pollution levels that have been demonstrated to be harmful but also to prevent lower pollutant levels that may pose an unacceptable risk of harm, even if the risk is not precisely identified as to nature or degree." Therefore, the charge in the most recent Integrated Science Assessment (ISA) supplement was to determine whether new scientific evidence indicated there is unacceptable risk of harm at $PM_{2.5}$ levels below the current standard of 12 $\mu g/m^3$.

It is clear to us that the summary of evidence provided by the US EPA, and contained within the Executive Summary of the 2019 ISA and its supplement, illustrates a continually growing and expanding body of scientific literature enumerating the many ways in which $PM_{2.5}$ is harmful to human health, including at levels below the current NAAQS, as

discussed below. We also note the need for the U.S. EPA to further evaluate the variability in $PM_{2.5}$ mass effects based on source and composition before the next Particulate Matter ISA.

ISEE NAC calls for lower concentration standards that would be consistent with the current state of the science and the Clean Air Act. Current scientific evidence clearly demonstrates a causal relationship of exposure to $PM_{2.5}$ at and below the current standard levels with several cardiovascular health outcomes, including death. Regarding the long-term standard, ISEE NAC has concluded that the available science clearly demonstrates that deaths and heart attacks are induced by $PM_{2.5}$ at concentrations between 8 and 12 $\mu g/m^3$. This evidence includes those already cited in the EPA's own 2019 Integrated Science Assessment (ISA) for Particulate Matter (2019 PM ISA)[2] and others that have been reported since the literature cutoff date for the 2019 PM ISA (approximately January 2018). In fact, the supplement to the 2019 PM ISA being developed by the EPA reports the studies of cardiovascular outcomes included in the 2009 PM ISA, the 2019 PM ISA, and recent studies published since the literature cutoff date of the 2019 PM ISA; with particular focus on ischemic heart disease (IHD), myocardial infarction (MI), and heart failure (HF). In support of the EPA's recent decision to reconsider the December 2020 decision to retain the current PM standards, we assert that the EPA should implement lower concentration PM standards based on existing epidemiological evidence. In support of our stance, we present the following epidemiological evidence for a causal relationship between PM exposure and health effects at or below 10 $\mu g/m^3$.

The Canadian Community Health Survey cohort studied 300,000 people across Canada.[3] The mean annual $PM_{2.5}$ concentration in the participants was only 6.3 $\mu g/m^3$, and the 95th percentile was 11.3 $\mu g/m^3$. They reported a strong association of $PM_{2.5}$ in that range and mortality rates. Moreover, the authors specifically examined whether there was a threshold at any concentration observed in their study and found none.

Di et al. examined the association of $PM_{2.5}$ concentrations below the EPA standard and mortality rates in 61 million Medicare beneficiaries over 13 years.[4] There were 247,682,367 person-years of follow-up and 11,908,888 deaths among participants with annual $PM_{2.5}$ concentration below 12 $\mu g/m^3$, and they also reported a strong association in that range.

More recently, Olaniyan et al.[5] assessed the incidence of acute myocardial infarction (AMI) and stroke hospitalizations in association with long-term exposure to $PM_{2.5}$. They used a large (N = 2.7 million) Canadian population-based national cohort study—the Canadian Census Health and Environment Cohort (CanCHEC).[6] They found that for AMI, each interquartile range (IQR) increase in $PM_{2.5}$ exposure was associated with a 2.6% increase in AMI incidence and a 7.8% increase in stroke incidence.[5] Of particular importance, the IQR used for their analysis was 3.27 $\mu g/m^3$; i.e., the increased risks in cardiovascular outcomes reported were observed at $PM_{2.5}$ concentrations that were much lower the current NAAQS standards: the 10-year moving average exposures to $PM_{2.5}$ for participants at baseline was 6.77 $\mu g/m^3$. Also, their findings were based on a model that fully adjusted for numerous individual and ecological covariates, and other pollutants.

Bai et al.[7] investigated the associations between exposure to $PM_{2.5}$ and other air pollutants and incidence of congestive heart failure (CHF) and acute myocardial infarction (AMI). They studied all long-term residents aged 35–85 years who lived in Ontario, Canada, from 2001 to 2015. They found that long-term exposure to $PM_{2.5}$ was associated with increased incidence of both congestive heart failure (CHF) and acute myocardial infarction

(AMI). In fully adjusted models, each increase of 3.5 μg/m3 in $PM_{2.5}$ was associated with a 5% increase in both CHF and AMI incidence. Again, these findings suggest that associations between $PM_{2.5}$ and major cardiovascular disease outcomes may be significant at concentrations much lower the current NAAQS standards.

Parker et al.[8] examined whether associations between $PM_{2.5}$ exposure and heart disease mortality differ by race/ethnicity. They used data from the 1997 to 2009 US National Health Interview Survey linked to mortality records.[9] They found a significant positive association between $PM_{2.5}$ and heart disease mortality. Overall, they estimated a 16% increase in mortality risk from heart disease for each increase of 10.0 $\mu g/m^3$ in $PM_{2.5}$. Interaction terms for non-Hispanic black and Hispanic groups compared with the non-Hispanic white group were not statistically significant.[8] Their analysis adjusted for several individual and contextual variables.

Cakmak et al.[10] analyzed the association between long-term $PM_{2.5}$ exposure and mortality due to ischemic heart disease, among other health conditions among members of the Canadian Census Health and Environment Cohort (CanCHEC).[6] They found each increase of 10 $\mu g/m^3$ in $PM_{2.5}$ was related to 13% risk of mortality due to ischemic heart disease. Their analysis adjusted for socioeconomic characteristics and other individual confounders.

Hayes et al.[11] examined the risks for cause-specific cardiovascular disease mortality in a large cohort (N = 565,477) of U.S. adult members of the NIH (National Institutes of Health)-AARP (American Association of Retired Persons) Diet and Health Study[12] with annual average $PM_{2.5}$ exposure. The authors ran fully adjusted models that accounted for several confounders and other known and suspected CVD risk factors (i.e., age, race or ethnic group, education, marital status, body mass index (BMI), alcohol use, smoking, median income, and percentage not completing high school in the census tract of residence at enrolment). They found that each increase of 10.0 $\mu g/m^3$ in $PM_{2.5}$ was associated with a 16% increase in the risk of mortality from ischemic heart disease and 14% increase in mortality risk from stroke. Important to the standard setting process, when $PM_{2.5}$ exposure of less than 8.0 $\mu g/m^3$ was used as the "standard" with which other exposure $PM_{2.5}$ profiles were compared, risks for CVD deaths statistically significantly increased by 4% for exposures in the range of 8–12 $\mu g/m^3$, 8% in the 12–20 μg/m3 range, and 19% for exposures above 20 $\mu g/m^3$ (vs. risk for those below 8 $\mu g/m^3$ $PM_{2.5}$ mean exposure).

Effects below 10 $\mu g/m^3$ were also confirmed in the study by Wu et al.,[13] who found elevated mortality rates in people exposed to 8-10 $\mu g/m^3$ $PM_{2.5}$, as compared to those exposed the concentrations below 8 $\mu g/m^3$. In a follow-up nationwide analysis, the authors focused on the relationship between long-term $PM_{2.5}$ exposure and mortality comparing numerous traditional and causal inference methods, leveraging the full nationwide US Medicare cohort (almost 70 million enrollees) who were linked to $PM_{2.5}$ exposures from the moment they entered the cohort until their death or the end of the study period (2016). The authors estimated that lowering the air quality standard to 10 $\mu g/m^3$ would save 143,257 lives (95% confidence interval, 115,581 to 170,645) in one decade[14].

Perhaps the most compelling evidence within the 2019 ISA Executive Summary itself is the conclusion that "evidence continues to support a linear, no-threshold concentration–response relationship, but with less certainty in the shape of the curve at lower concentrations (i.e., below about 8 $\mu g/m^3$)." (U.S. EPA, 2019, p. ES-23).[2] This statement suggests that at a minimum, annual averages of $PM_{2.5}$ between 8 -12 $\mu g/m^3$ may pose an unacceptable risk of

harm, and therefore a NAAQS annual standard closer to 8 μg/m^3 is most appropriate to propose. This conclusion would also be in line with Canada's recent decision to lower their $PM_{2.5}$ standard to 8.8 μg/m^3 in 2020, which had previously been set at 10 μg/m^3 in 2015. The Canadian targets were established based on the conclusion that, in the absence of population thresholds, CAAQS should incorporate an approach of continuous improvement. In fact, the Canadian standard of 8.8 was actually established in 2012, before many studies even showed associations of health effects with lower levels of $PM_{2.5}$.

We further note that the 2019 ISA and the supplement provide ample evidence that the current 24-hour standard of 35 μg/m^3 provides woefully inadequate public health protection, and also needs to be lowered.

In addition, regarding $PM_{2.5}$ source and composition, the PM ISA and supplement acknowledge these as factors in the variability of $PM_{2.5}$ health impacts, but do not sufficiently evaluate them as possible regulatory foci of further $PM_{2.5}$ regulation. Notably, the supplement acknowledges (on page 2-34) that "*Compared with the 2009 PM ISA, in which most epidemiologic studies of mortality conducted formal source apportionment analyses, studies evaluated in the 2019 PM ISA have focused more exclusively on $PM_{2.5}$ components. Of the limited number of studies that examined associations between short- and long-term source exposures and mortality, positive associations were observed for those sources representative of combustion-related activities, including traffic, coal, and vegetative fires.*" However, this important conclusion is not even mentioned in the ISA Supplement's Executive Summary, but should be, and this aspect also clearly needs more investigation by the EPA in its future monitoring, research, and standard setting efforts.

In conclusion, while the current NAAQS undoubtedly have reduced the burden of disease associated with air pollution, there is still significant room for improvement. For example, the EPA needs to accept the fact that $PM_{2.5}$ is causally related to lung cancer (not just "likely causal"). Indeed, the International Agency for Research on Cancer has declared "*There is sufficient evidence in humans for the carcinogenicity of particulate matter in outdoor air pollution. Particulate matter in outdoor air pollution causes cancer of the lung*" (IARC, 2016, p. 443).[15] The Global Burden of Disease Study has estimated that some 100,000 Americans die each year from $PM_{2.5}$ air pollution exposure at current levels[16]. Lowering the annual standard from 12 μg/m^3 to 8 μg/m^3 (the lower end of the proposed range, and close to the Canadian 2020 standard, albeit still higher than the most recent WHO guideline for $PM_{2.5}$) would substantially lower $PM_{2.5}$ pollution in the US and would, upon achieving compliance, avoid tens of thousands of needless deaths each year. Clearly, the longer the EPA delays taking action on lowering this $PM_{2.5}$ standard, the more American lives will be needlessly lost to this tiny, but toxic, public health menace.

Sincerely,

George D. Thurston, NYU School of Medicine, New York, NY
Abiodun Oluyomi, Baylor College of Medicine, Houston, TX

On behalf of the North American Chapter of the International Society for Environmental Epidemiology (ISEE)

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