Andrew Wheeler, Administrator
Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

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Re: $PM_{2.5}$ standard

Comments of the International Society for Environmental Epidemiology on EPA's decision to retain the current NAAQS standard for $PM_{2.5}$

The International Society for Environmental Epidemiology (ISEE) represents researchers who study environmental causes of ill health, including ambient air pollutants subject to the National Ambient Air Quality Standards (NAAQS) promulgated by EPA. We write in strong opposition to the EPA decision to retain the current $PM_{2.5}$ NAAQS standard. ISEE believes this decision is contrary to the state of the science, which clearly demonstrates that deaths and cardiovascular events, such as heart attacks, are produced by $PM_{2.5}$ at concentrations between 8 and 12 $\mu g/m^3$ and, hence, that the Administrator's decision violates the Clean Air Act requirement to use the "best available science" and to set standards "to protect public health with an adequate margin of safety." The current proposal does neither. Further, the conclusions put forth in the Administrator's proposed federal register notice are in direct contradiction to EPA's own internal scientific documents. ISEE favors a lower standard that would be consistent with the current state of the science and the Clean Air Act.

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) was to determine whether new scientific evidence indicated that there is unacceptable risk of harm at $PM_{2.5}$ levels below the current standard of 12 $\mu g/m^3$.

US EPA's ISA clearly documents 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. The Executive Summary concludes that recent and diverse epidemiologic studies continue to report consistent positive associations between short- and long-term $PM_{2.5}$ exposure and respiratory and cardiovascular effects and mortality, in some cases strengthening and extending the evidence base for other health effects.

ISEE concurs with this opinion as representing the state of the science. For example, regarding evidence for serious health effects below the current NAAQS, the Canadian Community Health Survey cohort studied 300,000 people across Canada.[1] 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 between $PM_{2.5}$ in that range and mortality rates. Moreover, the authors specifically examined whether there was a threshold concentration below which no effects were seen in their study and found none.

Another example is the report of Di et al., who examined the association of $PM_{2.5}$ concentrations below the EPA standard (12 $\mu g/m^3$) and mortality rates in 32.8 million Medicare beneficiaries over 13 years.[2] 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 these authors also reported a strong association between $PM_{2.5}$ in that range and mortality.

A 2017 paper studied 13 million residents of the Southeastern US from 2000–2013, and examined the association of $PM_{2.5}$ with death rates. When restricted to populations never exposed to 12 $\mu g/m^3$ or higher, they reported a significant association, and—as in the above studies—a steeper percent increase in death rates per one $\mu g/m^3$ increase in $PM_{2.5}$ than seen at higher concentrations.[3]

More recently, Hayes et al. evaluated the relationship of ambient $PM_{2.5}$ exposure with cause-specific cardiovascular disease (CVD) mortality in 565,477 US men and women, aged 50 to 71 years, from the well-characterized National Institutes of Health-AARP Diet and Health Cohort.[4] Compared with participants with $PM_{2.5}$ exposure < 8 $\mu g/m^3$ (referent concentration), risks for CVD mortality were statistically significantly increased among participants with $PM_{2.5}$ exposures in the range of 8–12 $\mu g/m^3$, documenting that significant adverse health effects are occurring in the US below the prevailing long-term $PM_{2.5}$ standard (12 $\mu g/m^3$) that the EPA claims to be sufficiently protective.

EPA has expressed a preference for studies examining whether changes in $PM_{2.5}$ cause changes in deaths or other adverse events and suggested such evidence is lacking. But Laden et al. specifically examined changes in $PM_{2.5}$ concentrations in two follow-up periods in the Harvard Six City Study and changes in mortality rates, and reported an association, with almost the same effect size as in the original study.[5] And a more recent study of Abu Awad et al. examined the change in $PM_{2.5}$ exposure due to moving residential location and changes in mortality experienced among people moving from the same neighborhood.[6] They also found a strong effect of higher levels of $PM_{2.5}$ on mortality.

The ISA addresses evidence of biological plausibility for PM health effects for the first time, as biological plausibility can strengthen causal inference. The Executive Summary found that a large number of animal toxicological and controlled human exposure studies provide coherence and biological plausibility for effects observed in epidemiologic studies of short- and long-term $PM_{2.5}$ exposure, particularly respiratory and cardiovascular effects, and mortality. In fact, studies that used concentrated ambient particle exposures provided evidence of a direct effect of PM exposure on various adverse health outcomes. The use of these other types of studies to help draw causal inference is not just the approach of EPA scientists, it is the standard in science. The ISA methods mirror those recommended by the National Academy of Sciences recent report to the Veterans Administration,[7] the World Health Organization[8] in their assessments of the effects of air pollution, the methods used by the American Heart Association in their review of the health effects of $PM_{2.5}$,[9] and by the Royal College of Physicians in their latest review of air pollution.[10] This is the standard for integrating knowledge across disciplines in science.

Nor is this evidence restricted to studies at high concentrations. For example, mice exposed to outdoor air with average $PM_{2.5}$ concentrations of 16.8 $\mu g/m^3$ had lower lung function than mice in the same location but exposed to filtered air.[11] A similar study (city air [22.1 $\mu g/m^3$] vs filtered air exposure) reported narrowing of the pulmonary arteries due to thickening of the walls and increased lung inflammation in the particle-exposed mice.[12] Yet another study confirmed this result and also found thickening of coronary arteries.[13] Therefore, this new evidence of biological plausibility further supports that $PM_{2.5}$ causally affects numerous health outcomes.

In addition, multiple studies, seemingly ignored by EPA, have used causal modeling methods to examine the effect of $PM_{2.5}$ on mortality and hospital admissions, including studies using difference-in-differences designs,[14–18] propensity scores,[6,19–22] and instrumental variables.[22–24] Combined with the substantial toxicological evidence the ISA has described, the evidence for causality of the mortality associations is overwhelming.

Previously identified weaknesses regarding lack of adjustment for co-pollutants were also addressed in this ISA and showed that adjustment for co-pollutants did not alter associations with $PM_{2.5}$. This, too, further strengthens causal inference. For example, the American Cancer Society Cohort examined the simultaneous association of $PM_{2.5}$, nitrogen dioxide (NO_2), and ozone (O_3) on mortality rates, and found continued association with $PM_{2.5}$,[25] as did the CANCHEC study.[26]

Perhaps the greatest evidence within the 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 $\mu g/m^3$)." 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 an annual national standard closer to 8 $\mu g/m^3$ would have been reasonable to propose. This conclusion would also be in line with Canada's recent decision to lower their $PM_{2.5}$ standard to 8.8 $\mu g/m^3$ in 2020, which had previously been set at 10 $\mu g/m^3$ in 2015. It is also consistent with a recent meta-analysis of 53 cohort studies which found significant associations between $PM_{2.5}$ well below 12 $\mu g/m^3$ and mortality[27] and directly attested to in the study of Wu,[19] who found elevated mortality rates in people exposed to 8–10 $\mu g/m^3$ $PM_{2.5}$ compared to those exposed the concentrations below 8 $\mu g/m^3$. The Canadian targets were established based on the conclusion that in the absence of population thresholds, Canadian Ambient Air Quality Standards (CAAQS) should incorporate an approach of continuous improvement. In fact, the Canadian standard of 8.8 $\mu g/m^3$—that came into effect in 2020—was actually established in 2012, before many studies even showed adverse associations of health effects at lower levels of $PM_{2.5}$.

The prior Clean Air Scientific Advisory Committee (CASAC) PM Committee, which was disbanded without notice on October 10, 2018, and which comprised a set of experts from diverse scientific disciplines such as epidemiology, toxicology, and human clinical studies, also found substantial evidence in favor of lowering the standard. Despite being disbanded, this independent former CASAC committee reviewed the ISA anyway, and concluded "the current suite of primary fine particle ($PM_{2.5}$) annual and 24-hour standards are not protective of public health." They suggested that the annual standard should be revised to a range of 10 $\mu g/m^3$ to 8 $\mu g/m^3$ whereas the 24-

hour standard should be revised to a range of 30 μg/m^3 to 25 μg/m^3. [28] This conclusion was based on consistent epidemiological evidence from multiple multi-city studies, augmented with evidence from single-city studies, at policy-relevant ambient concentrations, and are supported by research from experimental models in animals and humans and by accountability studies. These data provide clear and compelling scientific evidence that the current $PM_{2.5}$ standards are not adequate to protect human health and that EPA has ignored the "best available science."

Moreover, ISEE remains concerned about the litany of unwarranted changes the EPA has made to the CASAC and the NAAQS review process. The current CASAC is unqualified to interpret epidemiologic studies given that it lacks adequate depth and diversity of epidemiologic expertise. The myriad of changes to the NAAQS review process are collectively harmful to the quality, credibility, and integrity of the scientific review process and to the CASAC as an advisory body.

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. 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." 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. 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) 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 action on lowering the $PM_{2.5}$ standard, the more American lives will be needlessly lost to this tiny, but toxic, public health menace.

Sincerely,

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On Behalf of the
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