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Before

Clean Air Scientific Advisory Committee on the
Integrated Science Assessment for Fine Particulate Matter (PM2.5)
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Chairman Cox, and Members of the Committee, Good Morning, my name is Stewart Holm and I am Chief Scientist at the American Forest & Paper Association (AF&PA). I appreciate the opportunity to provide comments to the Clean Air Scientific Advisory Committee (CASAC) on the Integrated Science Assessment (ISA) for fine particulate matter (PM2.5).

The American Forest & Paper Association (AF&PA) serves to advance a sustainable U.S. pulp, paper, packaging, tissue and wood products manufacturing industry through fact-based public policy and marketplace advocacy. AF&PA member companies make products essential for everyday life from renewable and recyclable resources and are committed to continuous improvement through the industry's sustainability initiative — *Better Practices, Better Planet 2020*. The forest products industry accounts for approximately four percent of the total U.S. manufacturing GDP, manufactures over $200 billion in products annually and employs approximately 950,000 men and women. The industry meets a payroll of approximately $50 billion annually and is among the top 10 manufacturing sector employers in 45 states.

Determining whether there is a causal link between chronic exposure to PM2.5 and mortality is a fundamental challenge in supporting an appropriate National Ambient Air Quality Standard (NAAQS) for PM2.5. Much of my testimony is the result of an expert panel discussion held in June of 2017 on the importance of long-term epidemiology studies that indicate the presence of confounding when analyzed at the national scale. The discussion was organized by the Electric Power Research Institute and included Richard Bilonick (University of Pittsburg), Garrett Glasgow (NERA Economic Consulting) and Adam Szpiro (University of Washington).

EPA states that a causal relationship is one where the pollutant has been shown to result in health and welfare effects at relevant exposures based on studies encompassing multiple lines of evidence, and chance, confounding, and other biases

can be ruled out with reasonable confidence. This testimony will focus on EPA's evaluation of long-term exposure for total mortality, cancer, and cardiovascular effects where EPA's draft conclusions are causal, likely causal, and causal, respectively. Both EPA's causal and likely causal criteria require that systematic biases have been adequately controlled. Absent such control, causation is lacking. All that can be concluded after nearly three decades of associational cross-sectional research is that people live shorter lives that happen to live in cities with higher PM2.5. This falls short of demonstrating causality.

There are many studies that have reported a statistical association between PM2.5 and mortality. Most of these studies used time-invariant measures of PM2.5 ambient concentrations, not personal exposure, that did not vary across individuals and individual-level covariates were often collected once at baseline. Because of the many factors that vary across populations in disparate cities may be associated with both air pollution and mortality, the spatial information may be subject to confounding bias from unmeasured factors.

These cross-sectional studies can be vulnerable to confounding due to differences across the cities that may be correlated with PM2.5 exposure, such as socioeconomic or behavioral factors. Further, cross-sectional studies often do not address the influence of long-term time trends in both ambient PM2.5 levels and mortality. PM2.5 levels are decreasing across most of the U.S., while life expectancy is increasing. If the relationship between PM2.5 exposure and mortality is not causal, but PM2.5 concentrations and life expectancy follow similar trends, there can be a spurious relationship between exposure and mortality.

A recent paper by Pun et al. 2018, published in the American Journal of Epidemiology, examined the relationship between 12-month moving average PM2.5 and monthly mortality for a Centers for Medicare and Medicaid Services cohort of over 20 million individuals residing in ZIP codes with a geographic centroid within six miles of any one of 798 air quality monitors in the US from 2000 to 2012. This study which was not referenced by EPA in the ISA, examines the possibility of unmeasured confounding of the long-term association between PM2.5 exposure and mortality by decomposing PM2.5 into two orthogonal components: (1) a temporal component that measures the national trend in PM2.5, and (2) a spatio-temporal component that measures the local trend in pollution after controlling for the national trend.

Assuming that the relationship between PM2.5 exposure and mortality is linear, the coefficients on the temporal and spatio-temporal measures of PM2.5 should be similar. But, in fact, they were not. The Pun et al. study observed for the temporal data statistically-significant positive results for all-cause mortality, as well as total cardiovascular and total cancer mortality. Importantly, the coefficients for the spatio-temporal trend were smaller and statistically insignificant. This study also shows that PM2.5 and mortality are trending downward over time, leading to a large positive association between PM2.5 and mortality using the temporal data. However, areas with

steeper declines in PM2.5 do not have correspondingly steep declines in mortality. These findings indicate that the long-term relationship between PM2.5 and mortality is confounded by some other, unmeasured long-term trend(s). This lack of a clear and consistent long-term relationship between PM2.5 exposure and mortality raises questions about spatial confounding in the cross-sectional studies mentioned earlier.

Another important component of the Pun study was the performance of multivariable regression analyses to assess the association between mortality and PM2.5 without and with adjusting for potential confounding by behavioral covariates from the Selected Metropolitan/Micropolitan Area Risk Trends of the Behavioral Risk Factor Surveillance System (BRFSS). Pun specifically controlled for monthly county-level prevalence of non-whites, current smokers, diabetics, heavy drinkers, asthma, average median income, and body mass index. The variables were selected *a priori* based on their previous associations with either mortality or PM2.5.

In contrast to the Pun study is a recent paper using the Medicare database by Di et al., 2017, and published in the New England Journal of Medicine. This paper which EPA cited in the ISA, also looked at long-term exposure to air pollution. Di concluded that there was "significant evidence of adverse effects related to exposure to PM2.5 and ozone at concentrations below current national standards." Most of you have probably heard of or read this paper. With regard to behavioral activity or confounding, Di stated the following: "[s]ensitivity analyses showed that smoking and socioeconomic status are unlikely to confound the association, and we controlled for spatial variation (see the Supplementary Appendix, available with the full text of our article at NEJM.org)." It appears that Di summarily minimized the importance of these confounders.

On the other hand, Pun et al., Table 1 (web table 4 of the publication) presents findings for temporal and spatio-temporal while Table 2 presents findings for both BRFSS-adjusted and non-adjusted. Temporal data for both all-cause and cause-specific for the non-adjusted model is positive and statistically significant. On the other hand, spatio-temporal data for all-cause and cause-specific for the US are all much lower and statistically insignificant. Additionally, comparing temporal data for non-adjusted versus BRFSS-adjusted data shows that the adjusted outcomes are much lower effect estimates that are statistically insignificant, and some cause-specific outcomes have point estimates below 1. Keep in mind that the Di et al. study and the Pun et al. study presumably use the same data. If there is no residual confounding in the spatio-temporal comparisons over time, the association between PM2.5 and mortality should be approximately the same at the two scales. However, the Pun study finds very different associations between the two scales. Di, however, does not separately analyze these data at the two scales.

In summary, the Pun paper provides an approach that decomposes information from an observational epidemiologic study into distinct temporal and spatio-temporal components which reveal confounding bias. Most previous studies of long-term air pollution exposure have focused on the cross–sectional comparisons. In Pun,

comparisons are made over time, using each city as its own control. The result is a substantial difference in the estimated PM2.5 all-cause mortality as well as cause-specific mortality. Although both PM2.5 and mortality are trending downward nationally, cities with steeper reductions in PM2.5 do not tend to have steeper reductions in mortality. The Pun study illuminates the complexity and uncertainty in the studies at the heart of the PM2.5 debate. Until this uncertainty is addressed, it is possible that a substantial portion of the conclusions reached by the ISA regarding adverse health effects may be unreliable. Accordingly, we respectfully submit that the CASAC accept the Pun study and maintain the existing standard.

Table 1. Temporal and spatio-temporal mortality risk rations per 10 ug/m3 increase in 12-month moving average of PM2.5 exposure; non-adjusted model

Cause of Death	Temporal	Spatio-temporal
All-cause	2.051 (1.996, 2.107)	1.008 (0.578, 1.758)
All-cardiovascular	4.38 (4.194, 4.574)	1.012 (0.411, 2.495)
All-cancer	1.492 (1.409, 1.58)	1.017 (0.752, 1.376)

Table 2. Temporal non-adjusted and temporal adjusted for BRFSS

Cause of Death	Temporal Non-Adjusted	Temporal Adjusted
All-cause	2.051 (1.996, 2.107)	1.003 (0.988, 1.019)
All-cardiovascular	4.38 (4.194, 4.574)	0.992 (0.968, 1.016)
All-cancer	1.492 (1.409, 1.58)	0.997 (0.965, 1.031)

BRFSS-adjusted model: adjusting for county-level race (being non-white), smoking, diabetes, body mass index, alcohol consumption, asthma, and median income.