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VIA EMAIL AND U.S. MAIL

Dr. Holly Stallworth
Designated Federal Officer (DFO)
EPA Science Advisory Board (1400F)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW.
Washington, DC 20460

Re: Written Statement of the National Cattlemen's Beef Association and National Mining Association for the Clean Air Science Advisory Committee Teleconference on May 7, 2010, Regarding the Policy Assessment for the Review of the Particulate Matter National Ambient Air Quality Standards—First External Review Draft. 75 Fed. Reg. 19971 (April 16, 2010).

To the Members of CASAC and the Particulate Matter Review Panel:

On behalf of the National Cattlemen's Beef Association ("NCBA") and National Mining Association ("NMA"), we appreciate the opportunity to provide this written statement on the Environmental Protection Agency's Policy Assessment for the Review of the Particulate Matter National Ambient Air Quality Standards ("NAAQS")—First External Review Draft, 75 Fed. Reg. 4067 (Jan. 26, 2010), Docket No. EPA-HQ-OAR-2007-0492 ("Draft Policy Assessment"). EPA recently provided notice of the May 7, 2010 teleconference to further discuss the Draft Policy Assessment, and allowed for written statements to be submitted by May 1, 2010 for consideration by CASAC and the Particulate Matter Review Panel. 75 Fed. Reg. 19971 (April 16, 2010).

I. INTRODUCTION

NCBA and NMA represent the interests of agriculture and surface mining operations, many of which are located in rural regions of the western United States where coarse particulate matter ("PM coarse") fugitive dust predominates due to arid conditions. NCBA and NMA agree with the conclusion in the Draft Policy Assessment that the existing 24-hour national ambient air quality standards ("NAAQS") standard for PM_{10} should not be revised. As one of EPA's own health advisors has recognized, any reduction in the level of the current PM_{10} standard would shift to nonattainment those areas where rural coarse PM dominates without any evidence that this material causes harm to public health.

A. NCBA

Initiated in 1898, NCBA is the marketing organization and trade association for America's cattle farmers and ranchers. With offices in Denver and Washington, D.C., NCBA is a consumer-focused, producer-directed organization representing the largest segment of the nation's food and fiber industry. As representatives of family farmers and ranchers with a vested interest in protecting the environment, NCBA is pleased to provide the following comments.

NCBA represents tens of thousands of America's farmers, ranchers and cattlemen who provide much of the nation's supply of food. Its members are proud of their tradition as stewards and conservators of America's land, and good neighbors to their communities. They support dust control measures, ranging from soil conservation to fugitive dust control plans, which they carry out every day of every year in supplying America with the food it needs.

B. NMA

NMA is a national trade association of mining and mineral processing companies whose membership encompasses producers of most of the United States' metals, coal, uranium, and industrial and agricultural minerals; manufactures of mining and mineral processing machinery, equipment and supplies; and engineering consulting, transportation and financial institutions that provide services to the mining industry.

The broad contours of economic impact of PM_{10} regulation of PM coarse sources, particularly on western surface mining, have been considered in several proceedings, such as the adoption of PM_{10} Prevention of Significant Deterioration ("PSD") increments, and EPA's decision not to include surface coal mines in the PSD permit program. In those proceedings, EPA determined that a typical western surface mining operation would be prohibited by the PM_{10} increments. In the later proceeding, EPA determined not to include coal surface mines as listed PSD major sources, because the environmental benefit from doing so was outweighed by the adverse economic impact. 54 Fed. Reg. 48870 (November 28, 1989).

Because mines are already required to control coarse PM through a variety of technology and management requirements little more can be done to comply with a more stringent coarse PM NAAQS other than scale back or shut down operations. The impacts of a more stringent coarse PM standard to energy and commodities markets, not to mention the communities and ancillary businesses that depend on mining, would be substantial, sending ripple effects throughout the economy.

II. THE DRAFT POLICY ASSESSMENT SUPPORTS RETAINING THE CURRENT PM_{10} STANDARD

A. While PM_{10} as a Coarse PM Indicator is Confounded by the Presence of PM Fine, Retention of the Current PM_{10} Indicator Allows a Critical Distinction to be Made Between Urban and Rural Coarse Particles.

Both EPA and the Clean Air Science Advisory Committee ("CASAC") recognize PM coarse and PM fine as two distinct pollutants. PM fine is combustion-derived material that is composed of sulfates, organics, ammonium, nitrates, carbon, and lead, while PM coarse is crustal, mechnically-derived material made up primarily of naturally occuring earthen materials. Historically there has been no evidence of adverse health effects from coarse, crustal PM at ambient levels, (comments of NCBA and NMA on Integrated Science Assessment, Nov. 9, 2009, Docket 2007-0517), and EPA has recognized this critical distinction between fine and coarse PM by allowing exceptions to NAAQS compliance for rural fugitive dust. Moreover, EPA's regulation of PM has increasingly focused on the fine fraction (by the $PM_{2.5}$ standard), as the PM component of primary health concern.

Using PM_{10} as an indicator for coarse PM is problematic given that it includes both PM fine and PM coarse. As has been acknowledged in the scientific discussions of PM coarse, much of the evidence that is reviewed is actually PM_{10} data and, given the very different properties and effects of PM fine and PM coarse, it may well be that the PM fine component is what is actually causing the observed adverse effect, not the coarse fraction. Epidemiological studies of health effects resulting from PM_{10} do not (nor could they) differentiate between the observed health effects resulting from coarse PM and those resulting from fine PM ($PM_{2.5}$). Use of these studies to identify health effects for purposes of establishing a coarse PM standard is therefore inappropriate. Some individual members of CASAC have expressed concern with reliance on PM_{10} data:

> The concept that the abundant data on PM_{10} might serve to selectively support the causality determinations for $PM_{2.5}$ and $PM_{10-2.5}$ is problematic. As described above, PM_{10} contains both fractions and there will always be uncertainty as to whether effects measured in response to PM_{10} are related to the $PM_{2.5}$ fraction, the $PM_{10-2.5}$ fraction or some combination of the two.

CASAC Comment Letter on draft ISA, Individual Comments of Wayne Cascio (Nov. 2009). Furthermore, the conclusions of the epidemiologic studies that consider PM_{10} health effects are substantially less certain where they do not account for the potential for confounding by other gaseous co-pollutants. Very few studies consider this additional uncertainty, and where they do, the results are found to be statistically non-significant. Draft Policy Assessment, at 3-21, 3-22.

EPA's 2006 review of the PM NAAQS focused on regulating coarse PM despite the lack of health evidence for adverse effects from coarse PM, but posited that coarse PM found in urban areas might be of concern because of the potential for contamination by PM fine particles. Even that review round did not find direct adverse health effects from coarse PM at ambient levels. However, because of the concern with contamination from fine PM of urban coarse particles, EPA, nevertheless, determined to regulate coarse PM. EPA acknowledged that the health evidence for rural coarse PM (as distinguished from urban coarse PM) was uncertain but regulated it using the PM_{10} standard as a cautionary measure. PM_{10} was defended as the indicator for coarse PM despite its confounding by fine PM because it would, in theory, allow more coarse PM where fine PM levels were lower (rural areas) and less coarse PM where fine PM levels were higher (urban areas). In this way, the PM_{10} standard was justified as a way of targeting the coarse particles of concern, those in urban areas.

EPA continues to acknowledge the lack of evidence of adverse health effects from rural coarse PM at ambient levels in the Draft Policy Assessment, and concludes that this lack of health evidence supports retaining the current PM_{10} standard. The current PM_{10} standard allows for a differentiation between rural and urban coarse PM and an acknowledgement that there continues to be no evidence of adverse health effects from rural coarse PM. As the draft Policy Assessment states:

> [M]ost of the evidence for positive associations between $PM_{10\text{-}2.5}$ and morbidity and mortality, particularly evidence for these associations at relatively low concentrations of $PM_{10\text{-}2.5}$, continues to come from studies conducted at locations where the $PM_{10\text{-}2.5}$ is expected to be largely of urban origin.
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> *****
>
> [W]e note that varying levels of thoracic coarse particles allowed by a PM_{10} indicator would be expected to **target protection to those locations (i.e., urban or industrial areas) where the strongest evidence has been observed for associations between adverse health effects and exposures** to thoracic coarse particles. Therefore, under this approach to considering the evidence, a reasonable conclusion would be that a PM_{10} indicator remains appropriate for a standard meant to protect against exposures to thoracic coarse particles.

Draft Policy Assessment at 3-33 to -34 (emphasis added).

As recognized by the Integrated Science Assessment ("ISA") adopted in December of 2009, the most thorough and best quality studies considered since the 2006 review find no adverse health effects from ambient levels of coarse PM. ISA at 6.5.2.3. This is particularly true for rural coarse PM. Although EPA cites to several recent studies of dust storms as support for its statement that "caution is warranted in drawing conclusions about the relative toxicity of thoracic coarse particles from urban versus non-urban environments," Draft Policy Assessment at 3-32, as discussed below, the results of these studies do not confirm health risks from coarse PM at ambient levels that exist in rural areas of the United States:

- The only study of dust storms reaching North America, with hourly concentrations greater than 100 µg/m^3, found no additional risk of cardiac or respiratory hospital admissions. Bennett, "Impact of the 1998 Gobi dust event on hospital admissions in the Lower Fraser Valley, British Columbia", *Sci Total Environ*, 366: 918-925 (2006).

- The remaining studies cited by EPA involved high wind events with high hourly PM_{10} concentrations, which in one case approached 300 µg/m^3 to 400µg/m^3 with maximum 24-hour PM_{10} concentrations at 1,371 µg/m^3. Middleton, "A 10-year time-series analysis of respiratory and cardiovascular morbidity in Nicosia, Cyprus: the effect of short-term changes in air pollution and dust storms," *Environ Health*, 7:39 (2008).

- Furthermore, the majority of these studies involved Asian dust storms originating in the Gobi and Takla Makan deserts in Mongolia and western China, which travel across some of the most industrial areas of China. As a result of this route of transport, it is "likely that a certain amount of chemicals attached to the Asian dust may be from urban or industrial emissions in China." Chan, "Increasing cardiopulmonary emergency visits by long-range transported Asian dust storms in Taiwan," *Environ Res*, 106: 393-400 (2008).

These studies are not representative of ambient rural coarse PM levels in the United States and cannot be relied upon as indicators of health risks from coarse PM in rural areas of the arid West.

As imperfect as the PM_{10} indicator may be for regulating coarse PM (and the continuing concern that fine PM exposure continues to confound any reliable analysis of PM_{10} based epidemiological studies), we support its retention because of the critical need to recognize that there is simply no evidence of adverse health effects from ambient levels of rural coarse PM, the type of PM that predominates at agriculture and mining operations, especially those located in the arid west.

B. The Uncertainty in the Health Evidence Supports a Decision not to Revise the Level of the Coarse PM Standard.

While the Draft Policy Assessment attempts to put the best face on evidence that might be used to show PM coarse effects in areas with PM_{10} levels below the current standard and does not address contrary evidence that shows no effects, it does acknowledge the Integrated Science Assessment conclusions that "there is greater error in estimating ambient concentrations of $PM_{10\text{-}2.5}$ than in estimates for $PM_{2.5}$ and, therefore, that such uncertainty is a particularly relevant consideration when interpreting $PM_{10\text{-}2.5}$ epidemiologic studies." Draft Policy Assessment at 3-20.

Some of the uncertainties in the evidence noted by the ISA include: 1) exposure measurement error -- "there is greater spatial variability in $PM_{10\text{-}2.5}$ concentrations than $PM_{2.5}$ concentrations, resulting in increased exposure error for the larger size fraction" (Draft Policy Assessment at 3-21, quoting ISA at 3.5.1.1); 2) varying approaches used to measure $PM_{10\text{-}2.5}$ exposure; and 3) confounding by co-occurring pollutants.

As to item 2), varying approaches used to measure PM coarse exposure, the Draft Policy Assessment states:

> Uncertainty also results from the different approaches taken to estimate $PM_{10\text{-}2.5}$ concentrations in epidemiological studies. The ISA notes that ambient concentrations of $PM_{10\text{-}2.5}$ are generally determined by the subtraction of $PM_{2.5}$ from PM_{10} measurements with different studies using different methods….Given the use of these different approaches to estimating $PM_{10\text{-}2.5}$ concentrations across studies, and their inherent limitations, **the distributions of thoracic coarse particle concentrations over which reported health outcomes occur remain highly uncertain.**

Draft Policy Assessment at 3-21 (emphasis added). Some of these uncertainties stem from the reliance on data from co-located monitors rather than actual PM coarse data, and data from monitors that are located in separate and distinct areas, with differing exposures, from the areas with recorded hospital admissions. The use of central monitoring data is particularly problematic for PM coarse because, as EPA acknowledges, PM coarse falls out more rapidly from its source and central monitor measurements do not accurately reflect actual PM coarse exposures of the populations in the epidemiologic studies. As just one example, one of the new studies cited by EPA uses the difference between county-wide PM_{10} and $PM_{2.5}$ monitors to estimate coarse PM, an even grosser estimate of PM coarse exposures than the more typical co-located monitor subtraction approach. Zanobetti & Schwartz., "The effect of fine and coarse particulate air pollution on mortality: A national analysis," *Environ Health Perspect*, 117: 1-40 (2009); see the Comments of Dr. Jonathan Borak on the draft Integrated Science Assessment (Nov. 9, 2009), which focus in particular on the Zanobetti & Schwartz study and its significant, fundamental limitations (attached as Exhibit A).

As to item 3), confounding by co-occurring pollutants, the Draft Policy Assessment states:

> The ISA also notes that the potential for confounding by co-occurring pollutants has been addressed in only a relatively small number of $PM_{10\text{-}2.5}$ epidemiologic studies, introducing additional uncertainty into the interpretation of these studies. ISA at 2.3.3. As discussed above, most studies that have evaluated co-pollutant models have reported that $PM_{10\text{-}2.5}$ effect estimates remain positive, but often lose precision and **become statistically non-significant**.

Draft Policy Assessment at 3-21 (emphasis added). These co-pollutants include $PM_{2.5}$ confounding, as well as confounding from gaseous pollutants. Once these co-pollutants are considered in the few studies that have indicated adverse health effects from coarse PM, the effect estimates become statistically non-significant – no more likely to occur than not occur. Epidemiological studies of health effects resulting from PM_{10} do not (nor could they) differentiate between the observed health effects resulting from coarse PM and those resulting from fine PM ($PM_{2.5}$). Use of these studies to identify health effects for purposes of establishing a coarse PM standard is therefore inappropriate. As one member of CASAC stated, "the extent to which PM_{10} reflects $PM_{2.5}$ . . . may make it insurmountably problematic in using it for reviewing evidence and deliberating on the level of standard to protect against effects of $PM_{10\text{-}2.5}$." Comments from Dr. Sverre Vedal, Preliminary Individual Comments (as of Apr. 7, 2010) on Draft Policy Assessment.

Finally, as acknowledged by EPA in the Draft Policy Assessment, experimental support for the conclusions reached by the epidemiologic studies is limited:

> Controlled human exposure studies have not reported effects of thoracic coarse particles on pulmonary endpoints including lung function or respiratory symptoms. In addition, toxicological studies have not generally assessed inhalation of coarse thoracic particles due to the technical challenges associated with conducting $PM_{10\text{-}2.5}$ inhalation study in rodents …. and so provide only limited biological plausibility for the associations reported in epidemiologic studies.

Draft Policy Assessment at 3-10.

Importantly, too, EPA concluded that the evidence for coarse PM was so uncertain that it could not be used in a risk assessment, a typical method by which NAAQS levels are set. As EPA noted in the Draft Policy Assessment:

> Staff concluded that limitations in the monitoring network and in the health studies that rely on that monitoring network, which would be the basis for characterizing $PM_{10\text{-}2.5}$ exposures and risks, would introduce significant uncertainty into a $PM_{10\text{-}2.5}$ risk assessment such that the risk estimates generated would be of limited utility in performing review of the standard. Therefore, staff concluded in the second draft RA that a quantitative risk assessment for $PM_{10\text{-}2.5}$ is not supportable at this time.

Draft Policy Assessment at 3-7 (quoting second RA at 2-6). Thus, for all of the reasons discussed in more detail above, EPA staff concluded that the evidence of adverse health effects from coarse PM arising from the epidemiological studies was so uncertain that a risk assessment of $PM_{10\text{-}2.5}$ could not be conducted. This inability to conduct a risk assessment further supports EPA's view in the Draft Policy Assessment that the evidence is too uncertain to justify any change in the level of the current PM_{10} standard.

Considering all of these uncertainties in the coarse PM health evidence, the Draft Policy Assessment concludes:

> To the extent a decision on the adequacy of the current PM_{10} standard were to emphasize the uncertainties that contributed to the ISA conclusion that the evidence is "suggestive" of a causal relationship for $PM_{10\text{-}2.5}$ rather than indicating a "likely causal" or "causal" relationship [as was done for $PM_{2.5}$], **it would be reasonable to conclude that the available evidence does not provide a basis for reaching a fundamentally different conclusion from the one reached in the previous review (i.e., to retain the current 24-hour PM_{10} standard).**

Draft Policy Assessment at 3-25 (emphasis added). NCBA and NMA believe that any fair consideration of the PM_{10} standard must give due weight to the substantial uncertainties in the health evidence. We believe, if anything, the uncertainties and inadequacies in the existing health evidence for coarse PM are understated in both the ISA and the Draft Policy Assessment. Both documents fail to adequately discuss or characterize evidence. When evidence that actually shows no harm from ambient levels of coarse PM (indeed, in some studies, very high levels) is added to the significant uncertainties that EPA itself acknowledges in the health evidence, we believe there is no considered, health-based ground for reducing the level of the current coarse PM standard. Moreover, as one of EPA's own health advisors recognized, any reduction in the level of the current PM_{10} standard would put into nonattainment those areas where rural coarse PM dominates; this would result in requirements to control rural coarse PM and not urban coarse PM, when it is the rural coarse PM for which the health evidence is most uncertain.

III. CONCLUSION

EPA, in both the final ISA and the Draft Policy Assessment, acknowledges the substantial scientific uncertainties with linking coarse PM and health effects. Unlike $PM_{2.5}$, for which EPA concludes there is a "likely" causal relationship between short-term exposure and health effects, EPA finds that the relationship between short-term coarse PM exposure and health effects is merely "suggestive." Moreover, there is simply no evidence that rural coarse PM of the type associated with agriculture and surface mining operations poses any adverse risks to human health or the environment at ambient levels. For all of these reasons, NCBA and NMA support the conclusions by EPA in the Draft Policy Assessment that the existing 24-hour standard for coarse PM should not be revised.

Respectfully Submitted,

Denise W. Kennedy, P.C.
of Holland & Hart LLP

Attorneys for National Cattlemen's Beef Association
and National Mining Association

Enc.: Exhibit A

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Comments on:
Integrated Science Assessment for Particulate Matter – Second External Review Draft (July 2009)

Jonathan Borak, MD, DABT, FACP, FACOEM, FRCPC

November 9, 2009

I have prepared the following comments at the request of the National Cattlemen's Beef Association, the National Mining Association, and the Newmont Mining Corporation in order to share my concerns about the scientific interpretations and judgments that have apparently been adopted by EPA in the Second External Review Draft of the Integrated Science Assessment for Particulate Matter (July, 2009).

To introduce myself, I am Clinical Professor of Epidemiology & Public Health and Clinical Professor of Medicine at Yale University. I teach required graduate courses in both Toxicology and Risk Assessment. I also served for 10 years as a founding member of EPA's National Advisory Committee on Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL).

This is the fourth set of comments that I have submitted on issues related to the development of an NAAQS for coarse particulate matter ($PM_{10-2.5}$). Two earlier sets of comments were submitted to the Clean Air Scientific Advisory Committee in 2005 and one set to Administrator Johnson in 2006. Then as now, my principal concern is the lack of scientific support for a coarse particulate matter standard.

In these comments, I will focus on the informational limitations and uncertainties of the recent study by Zanobetti and Schwartz (Z&S) [1], a study that seems to play an inordinately important role in the draft ISA. As published and included in the ISA, that study suffers from the following important limitations and uncertainties:

1. The numbers of deaths in the $PM_{10-2.5}$ analyses are not described
2. The $PM_{10-2.5}$ data are subject to unquantified uncertainty
3. The effects of potential confounders and collinearity were not considered
4. The criteria for model selection are not adequately described and only a small minority of results was reported
5. The analytical results are inconsistent
6. The analytical findings cannot be generalized

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[1] Zanobetti A, Schwartz J: The effect of fine and coarse particulate air pollution on mortality: A national analysis. *Environ Health Perspect* 117:898-903, 2009

EXHIBIT A

In the following paragraphs I discuss these concerns in more detail. Ultimately, it is not possible to know whether these limitations reflect inadequacies of the research or its reporting, but in either case the report is not adequate to provide the basis to justify promulgation of a NAAQS for $PM_{10-2.5}$.

1. The numbers of deaths in the $PM_{10-2.5}$ analyses are not described

In their published report, Z&S reported the following information regarding mortality data used in their analysis:

> "In the 112 cities during the study period 1999-2005, there were 5,609,349 total deaths, 1,787,078 for CVD, 397,894 for MI, 330,613 for stroke, and 547,660 for respiratory disease." (p. 900)

This data set seems impressively large and precisely described, but that is not the number of deaths in the analysis. Cities were included in the study if there were exposure data for at least 265 days in a given year and, as documented in the Supplemental Material, many cities were not included for the full study duration. The actual numbers of study days included for each city are not provided. Based on the exclusion of years and days, it is apparent that the actual mortality data were significantly less than reported.

Of greater concern is the fact that only 47 cities were included in the $PM_{10-2.5}$ analyses, of which only 11 (23.4%) were included for the full duration, i.e., 1999-2005. Because the authors provided the average daily numbers of deaths by city, but not the number of days that each city was included in the study, it is not possible to estimate the actual numbers of deaths included in the $PM_{10-2.5}$ analysis. Of the nine cities with the highest daily all cause mortality (i.e., >40/day), $PM_{10-2.5}$ data were available for only four and none was included for the full duration of the study.

In summary, the study report overstates the quantity of mortality data that were included in the analyses. Presumably specific daily mortality data, not average daily data, were included in the time-series analytical model, but those data were not reported and cannot be calculated from the supplemental material. Likewise, the distributions of city-specific mortality were not described.

2. The $PM_{10-2.5}$ data are subject to unquantified uncertainty

2.a Uncertainties due to sampling methods

Environmental data for $PM_{2.5}$ and PM_{10} were obtained from the EPA Air Quality System and $PM_{2.5-10}$ values were calculated using the difference method. It is not clear whether Z&S considered the technical limitations of the data that resulted from differing sampler flow rates and differing collection conditions. The following describes the manner in which EPA addressed those concerns in its assessment of spatial distributions:

> "Since $PM_{10-2.5}$ is not routinely measured and reported to AQS, co-located PM_{10} and $PM_{2.5}$ measurements from the AQS network were used to investigate the spatial distribution in $PM_{10-2.5}$. Only low-volume FRM or FRM-like samplers were considered in calculating $PM_{10-2.5}$ to avoid complications with vastly different sampling protocols (e.g., flow rates) between the independent PM_{10} and $PM_{2.5}$ measurements … $PM_{2.5}$ concentrations are reported to AQS at local conditions whereas the PM_{10} concentrations are reported at standard conditions. Therefore, prior to calculating $PM_{10-2.5}$ by subtraction, the PM_{10} AQS data were adjusted to local conditions on a daily basis using temperature and pressure measurements from the nearest National Weather Service station." (ISA, p. 3-64)

There is no indication in their report that Z&S adjusted for differing flow rates or otherwise excluded samplers that were not "low-volume FRM or FRM-like" and there is no indication that they adjusted PM_{10} data to local weather conditions.

If Z&S did not exclude high-flow samplers and if they failed to adjust PM_{10} to local weather conditions, then their exposure data fall below the qualitative standards that EPA adopted for its own $PM_{10-2.5}$ studies.

2.b Uncertainties due to data averaging and regional distributions of coarse PM

Environmental data for $PM_{2.5}$ and PM_{10} were obtained at county levels, not for the cities *per se*. Where a city's population extended "beyond the boundaries of one county", the data from those several counties were aggregated. When more than one monitor was available, the results were averaged, but monitors that were not "well correlated" ($r<0.8$) with others in the county (or counties) were excluded. The proximity of monitors to the study's urban populations was apparently not considered, i.e., proximate monitors were not favored over distant ones, and distance was apparently not a criterion for excluding monitors.

This method raises a number of concerns. Z&S acknowledged that some study populations lived far from the monitors:

> "One possible explanation for the lower effect in the Mediterranean region … is more measurement error due to the extremely large counties in California, where people may live far away from the monitors." (p. 901)

This is of particular relevance because it is generally accepted that coarse PM deposits more rapidly and more locally than does fine particulate. Likewise, it is generally accepted that local sources are of greater importance in determining concentrations of coarse particulate. [2] Thus, one should expect that data from "far away" monitors will less accurately represent regional exposures to coarse particulate than fine particulate (e.g., $PM_{2.5}$). Measurements of coarse PM obtained at relatively distant monitoring stations (or calculated from PM_{10} data obtained at distant monitoring stations) should be

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[2] Burnett RT et al: Association between short-term changes in nitrogen dioxide and mortality in Canadian cities. *Arch Environ Health* 59:228-236, 2004.

viewed with caution, and caution is also necessary when evaluating studies that rely on $PM_{10-2.5}$ measurements obtained relatively far from target populations.

When such distant measures are used as the basis for epidemiological studies, efforts should be made to demonstrate that the distant measures accurately reflect the actual exposures of target populations. This specific concern undercut the probative value of the Detroit study by Lippman et al. [3]. The failure of Z&S to demonstrate that calculated $PM_{10-2.5}$ measurements reflected the actual exposures of the study's urban populations raises important concerns about the study's informative value.

The ISA discounts the significance of this concern, asserting that such measurement errors would lead to nondifferential misclassification which, in turn, would bias results toward the null:

> "Because of the greater spatial heterogeneity of $PM_{10-2.5}$, exposure measurement error is more likely to bias health effect estimates towards the null for epidemiologic studies of $PM_{10-2.5}$ versus PM_{10} or $PM_{2.5}$, making it more difficult to detect an effect of the coarse size fraction." (p. 6-131)

However, a recent EPA study in Phoenix contradicted that view. Wilson et al.[4] found that increasing distance from a central monitor was associated with an increasing positive association of $PM_{10-2.5}$ with cardiovascular mortality:

> "The % risk and statistical significance for the association of mortality with $PM_{2.5}$ fell off with distance from the monitor, as would be expected if exposure error increased with distance. However, the % risk for $PM_{10-2.5}$ increased …" (p. S11)

Thus it should be apparent that the biasing effects of measurement errors, such as those likely to have been present in the Z&S data, cannot be simply discounted on the presumption that such errors will necessarily lead to negative bias. To the contrary, as seen in Wilson et al[4], they can lead to positive bias and incorrect inferences of causality.

A further concern is the exclusion of monitors that were not "well correlated" with other county monitors, which thereby resulted in exclusion of an unstated amount of data. It would be important to know whether any of the excluded monitors were actually closer to, and therefore more representative of the population in any of the study cities, than the monitors that were included. It would also be useful to know how many monitors and how much data were excluded in this way.

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3 Lippmann M, et al: Association of Particulate Matter Components with Daily Mortality and Morbidity in Urban Populations. Cambridge: Health Effects Institute, 2000; Ito K. Associations of particulate matter components with daily mortality and morbidity in Detroit, Michigan. In: *Revised Analyses of Time-series Studies of Air Pollution and Health*, Boston: Health Effects Institute, pp. 143-156, 2003.

4 Wilson WE et al: Influence of exposure error and effect modification by socioeconomic status on the association of acute cardiovascular mortality with particulate matter in Phoenix. *J Expo Sci Environ Epi* 17:S11-S19, 2007.

3. The effects of potential confounders and collinearity were not considered

3a. Bias due to confounding

Z&S performed single pollutant analyses for $PM_{2.5}$ and $PM_{10-2.5}$ and they also performed two-pollutant analyses that included both $PM_{2.5}$ and $PM_{10-2.5}$. They did not consider the confounding effects of gaseous pollutants and they did not consider the probable collinearity between $PM_{2.5}$ and $PM_{10-2.5}$.

Reliance on single pollutant models substantially reduced the probative value of the resulting analysis. The ISA describes the failure to investigate confounding by gaseous copollutants as a "limitation" of the study (p. 6-301). A more general statement of concern is found in a report by the HEI Research Committee, which expressed the view that single-pollutant models provide only limited insights [5]:

> "In order to determine the relative effects of several risk factors on a health outcome, ideally all variables under considerations would be included in a single model."

An even stronger viewed was made by Klemm and colleagues who proposed that single-pollutant models can serve as screening tools, but are not a valid basis for determining the importance of any given pollutant [6]:

> "It is axiomatic … single-pollutant regressions may be a useful screening tool but cannot provide valid judgments as to the relative importance of a given pollutant." (p. 134)

Beyond such methodological concerns, there are empiric data that document confounding by gaseous copollutants in PM studies. Numerous studies, for example, have reported important confounding of coarse PM by NO_2 for both hospitalizations and mortality. For example:

> A significant effect of $PM_{10-2.5}$ on hospital admissions for respiratory diseases was reported in Toronto when a single-pollutant model was used, but the effect "was eliminated" when NO_2 was included in the analysis model. [7]

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[5] HEI Research Committee Comments in: Lippmann M, et al: *Association of Particulate Matter Components with Daily Mortality and Morbidity in Urban Populations*. Cambridge: Health Effects Institute, 2000; p. 80.

[6] Klemm RJ, et al: Daily mortality and air pollution in Atlanta: Two years of data from ARIES. *Inhal Toxicol* 16(suppl 1):131-141, 2004.

[7] Burnett RT, et al: The role of particulate size and chemistry in the association between summertime ambient air pollution and hospitalization for cardiorespiratory. *Environ Health Perspect* 105:614-620, 1997.

> In a study of 12 Canadian cities, apparent associations of $PM_{10-2.5}$ with mortality were seen in a single pollutant model, but were reduced by more than 50% and became non-significant when NO_2 was included in dual-pollutant model. [2]

> In a subsequent pooled analysis of ten Canadian cities, which may have used an overlapping dataset, NO_2 had the strongest association with non-accidental mortality. Apparent effects of PM became non-significant when NO_2 was included in the analytical model. [8]

Because the limitations of single-pollutant regressions are so well recognized, and because confounding of PM studies by NO_2 has been well documented, it is surprising that the ISA has given such prominence to this study, which generally failed to consider gaseous copollutants and specifically failed to consider confounding by NO_2.

Moreover, previous studies (e.g., Burnett et al. [2]; Brook et al. [8]) have reported that NO_2 was associated with seasonality effects similar to those reported by Z&S for $PM_{10-2.5}$. Thus, it seems possible that both the magnitude of the $PM_{10-2.5}$-associated mortality effects reported by Z&S and also the seasonality of these effects are attributable to confounding by NO_2. It is unfortunate that such possibilities were not explored.

3b. Bias due to collinearity

Z&S included $PM_{2.5}$ and $PM_{10-2.5}$ in a two-pollutant model, but they did not evaluate their possible collinearity. This specific concern was raised in the ISA:

> "models that include both PM10-2.5 and PM2.5 may suffer from instability due to collinearity." (p. 6-131)

Such collinearity would raise the possibility that risks were double-counted. It is unfortunate that such possibilities were not explored.

4. The criteria for model selection are not described and only a minority of results was reported

4.a Model selection

Z&S reports results for their time series analyses using PM concentrations averaged over the day of death and prior day (lag01):

> "We investigated the association between $PM_{2.5}$ and PM coarse concentrations averaged over the day of death and day before death and mortality with a time series analysis." (p. 899)

[8] Brook JR et al: Further interpretation of the acute effect of nitrogen dioxide observed in Canadian time-series studies. *J Expo Sci Environ Epi* 17:S36-S44, 2007.

It is apparent that they also performed numerous other analyses. For example, the refer to a "distributed lag model for 4 days, from the same day and up to 3 days earlier" and Figure 2 graphically presents cause-specific mortality data for each of 4 days (i.e., lag days 0-3). It seems likely that at least five different lag models were explored, but that the only data actually reported were from the lag01 analysis. Z&S also described a number of other variable aspects of their model fitting, including treatments for seasonality, ambient temperature, and day-of-the-week. The authors did not indicate whether they explored the effects of varying the numbers of degrees of freedom in their smoothing procedures; a recent report demonstrated that such decisions can significantly affect analytical results. [9]

It seems probable that numerous models, perhaps many, were fit to the data before a "best fit" model was chosen for the report. It is thus likely that analyses were performed repeatedly, with numerous alternative combinations and choices of parameters and adjustments and smoothing algorithms, but only a very limited set of results was presented. If this is correct, then it raises concerns about overestimation bias due to multiple tests and comparisons.[10]

Because the raw data were not provided, the extent and types of alternative analyses performed were not described, and the results of alternative analyses were not presented, the reported results must be viewed with caution. It seems likely that numerous analyses were performed on this dataset, but only the strongest result reported, thus the findings seem appropriate only for hypothesis generating, not hypothesis testing.

4.b Only a minority of results was reported

The failure to report most of the analytical data can be viewed from another perspective. Z&S analyzed mortality in 47 cities, considering overall mortality plus four mortality sub-categories. They also analyzed those data for each of four seasons plus all seasons combined.

Thus for each lag model, there were 235 individual city results for mortality categories (i.e., 47 (cities) x 5 (mortality categories) = 235) and when seasonality categories were included there were five times as many individual results (i.e., 47 (cities) x 5 (mortality categories) x 5 (season categories) = 1175), where each individual result represented a unique combination of [city-death category-season category]. In addition, for each lag model there were another 26 results representing the averages of those [city-death category-season category] groupings, for a grand total of 1201 analytical results per model.

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[9] Peng RD et al: Seasonal analyses of air pollution and mortality in 100 US cities. *Am J Epidemiol* 161:585-594, 2005.

[10] For example, see Jeffries NO: Multiple comparisons distortion of parameter estimates. *Biostatistics* 8:2500-504, 2007.

If five different lag models were explored, then there would have been more than 6000 results, reflecting individual combinations of [city-death category-season category-lag model]. However, the Z&S report included only 26 results for $PM_{10-2.5}$ (Table 2).

Z&S also stratified cities into six "climate classifications", which further increased the number of analytical results. In their report, they presented only 30 results, reflecting six "climate classifications" and five death categories for one lag model (Table 4).

Because detailed results were not reported, it is not possible to evaluate the consistency of the reported findings across the various cities and seasons, nor is it possible to estimate the uncertainty that characterized those findings. The aggregated results would be substantially less informative if no associations or negative associations with $PM_{10-2.5}$ had been seen in a large proportion of the individual cities. Ultimately, the probative value of these data depends on both the magnitude and consistency of the observed associations.

5. The analytical results are inconsistent

The findings reported by Z&S raise concerns about apparent inconsistencies. Although the report did not include city-specific findings, significant between-city heterogeneity was reported for overall mortality during spring, summer and autumn. Significant heterogeneity was also reported for respiratory mortality during the spring, when the largest positive effect of $PM_{10-2.5}$ was seen. Such heterogeneity suggests that there was a wide range of city-specific findings, with some cities showing no effects and perhaps others with significant negative effects. However, because the actual results were not provided, it is not possible to evaluate these possibilities.

The finding that $PM_{10-2.5}$ has adverse effects mainly during the spring, but not in other seasons is challenging. Z&S speculate that this reflects greater indoor PM penetration during the spring, but they also note that their findings are at variance with a recent NMMAPS report that found a different seasonal distribution of PM_{10}-related mortality in 100 US cities. [9]

The ISA also noted inconsistencies within the Z&S report and between the associations reported by Z&S and the results previously reported by others:

> "An examination of $PM_{10-2.5}$ mortality associations on a national scale found a strong association between $PM_{10-2.5}$ and respiratory mortality, but this association varied when examining city-specific risk estimates (Z&S, 2009). Additionally, copollutant analyses were not conducted in this study, and the associations observed are inconsistent with those reported in single-city studies." (p. 6-246)

In addition, Z&S reported that $PM_{10-2.5}$ was not associated with any effects in the area classified as "dry", a climate area that includes the cities of Phoenix and Albuquerque: "there was no effect in the dry region" (p. 901). But, as noted in the ISA, that finding is inconsistent with the results of at least four other studies:

"The lack of a $PM_{10-2.5}$-mortality association in the 'dry' region in this study is in contrast to the result from three studies that analyzed Phoenix data and found associations, as reviewed in the 2004 PM AQCD, and Wilson et al." (6-294)

6. The analytical findings cannot be generalized

The plausibility of the Z&S analytical findings rests on a series of hypotheses and speculations:

The absence of effects in the "Mediterranean region" (i.e., California, Oregon and Washington) might have been due to measurement error because the counties are so large.

The greater effect in spring might have been due to greater penetration of PM into residences.

The regional variation of $PM_{10-2.5}$ effects suggests "regional variations in the toxicity of coarse particles" which requires "further study".

Each of these hypotheses might prove correct, but none has been evaluated and the data needed to independently evaluate them has not been provided.

Thus, these study findings seem inconsistent across seasons, inconsistent between cities, and inconsistent with other published studies. For such reasons, the findings do not provide the basis to generalize, i.e., to describe the risks of $PM_{10-2.5}$ at a national level. The study successfully generates a variety of PM-related hypotheses, but unfortunately it fails to test those hypotheses and it does not serve as a sufficient basis to justify promulgation of an NAAQS.

Summary

The recent Z&S study represents a major effort to evaluate possible associations between $PM_{10-2.5}$ and mortality. It is unfortunate that this report does not allow such associations to be reasonably determined. It should be clear that the findings described in the June, 2009 issue of *Environmental Health Perspectives* leave many unanswered questions and they are not adequate to justify promulgation of a $PM_{10-2.5}$ NAAQS or support any revision to the PM_{10} NAAQS. To the contrary, the plausibility of the findings remains uncertain.

In the interest of understanding the adverse effects of exposure to coarse PM and in order to make full use of the Z&S data, I encourage EPA to ask HEI to review and comment on the data set and the analytical methods, and perform reanalysis if appropriate. It would be a shame to waste the efforts that Z&S have already made, but it would be worse to act on the basis of their published findings.