

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

**Compendium of Preliminary Pre-Meeting Comments  
CASAC Particulate Matter Review Panel on  
PM Integrated Science Assessment (First External Review Draft, Dec. 2008)**

<b>Comments from Dr. Lowell Ashbaugh</b> .....	2
<b>Comments from Mr. Ed Avol</b> .....	5
<b>Comments from Dr. Wayne Cascio</b> .....	9
<b>Comments from Dr. Ellis Cowling</b> .....	35
<b>Comments from Dr. James Crapo</b> .....	40
<b>Comments from Dr. Douglas Crawford-Brown</b> .....	42
<b>Comments from Dr. David Grantz</b> .....	46
<b>Comments from Dr. Joseph Helble</b> .....	51
<b>Comments from Dr. Rogene Henderson</b> .....	54
<b>Comments from Dr. Phil Hopke</b> .....	55
<b>Comments from Dr. Mort Lippmann</b> .....	59
<b>Comments from Dr. William Malm</b> .....	64
<b>Comments from Dr. Robert Phalen</b> .....	69
<b>Comments from Mr. Rich Poirot</b> .....	72
<b>Comments from Dr. Ted Russell</b> .....	83
<b>Comments from Dr. Frank Speizer</b> .....	86
<b>Comments from Dr. Helen Suh</b> .....	97
<b>Comments from Dr. Sverre Vedal</b> .....	101

## **Comments from Dr. Lowell Ashbaugh**

### Review of Chapter 9 – Ecosystem and Welfare Effects

#### Charge questions

1. How useful and complete is the scientific evidence presented and summarized in Chapter 9 regarding the effects of atmospheric PM on the environment, including (a) effects on visibility, (b) effects on individual organisms, (c) direct and indirect effects on ecosystems, (d) effects on materials, and (e) effects on climate? To what extent do the discussions and integration of evidence correctly represent and clearly communicate the state of the science?
2. This first external review draft PM ISA is of substantial length and reflects the copious amount of research recently conducted on PM. EPA has attempted to succinctly present and integrate the policy-relevant scientific evidence for the review of the PM NAAQS. Does the Panel have opinions on how the document can be shortened without eliminating important and necessary content?

The authors of this chapter have done an excellent synthesis of the relevant science regarding the effects of atmospheric PM on the environment. Some sections require technical editing for grammar and spelling, but the technical evidence is complete and is presented well. The presentation could be made more useful in several ways.

The spatial distribution of aerosol extinction and contribution of species to extinction in Figures 9-7 through 9-23 would be more useful if the contour intervals were standardized for groups of related figures. As they are presented they show the spatial patterns well but standardized intervals and ranges would also illustrate the temporal changes. If it makes sense to standardize the different species it would also better illustrate the relative impact of the different species in different time periods. If the levels for each species are too different, it would still be helpful to standardize the scales for each time period of a given species. It's also not clear on these figures why the highest contour level has a different spacing than the others. That makes the red (highest) contour levels misleading.

The sentence on lines 3-5 of page 9-31 is not clear. It's either a run-on sentence or is missing a crucial piece that would tie it together.

Because Figures 9-12 and 9-13 (also 9-14 & 9-15 and 9-16 & 9-17), are compared in the text, it would be helpful to place each pair on the same page or on facing pages so the reader can visually compare them more easily.

In the discussion comparing IMPROVE and CSN data, there should be some mention of the different methods of handling blank subtraction. IMPROVE subtracts a blank from each sample for ions and carbon analyses, but CSN does not. This makes comparing the concentrations between the networks a little more difficult; not impossible, but not straightforward.

The discussion of IMPROVE and CSN carbon data should comment on the different methods used to obtain the fractions. In fact, the discussion of carbon measurements in any network should include the method used to make them and how that may affect the results. Comparison of total carbon between networks is less sensitive to the method used, but comparison of the fractions is highly dependent on the method.

The statement on lines 7-8 of page 9-40 regarding fine soil and coarse mass is not entirely correct. The different ratio suggests a different composition of coarse mass but does not necessarily suggest a difference in the size distribution of suspendable soil materials. The statement is valid only if the assumption is true that fine soil is a good surrogate for coarse mass. In my experience that is just not true at all.

There is a mention on page 9-40 of the confounding effect of meteorologically driven interannual variability, but I would like to see an explicit statement calling for the investigation of the meteorological and climate-driven effects on particle concentrations and speciation. This is particularly relevant for the comment on page 9-44 regarding the depression of wintertime particulate nitrate for several years measured by the IMPROVE network. This feature may be due to meteorological influences, but has not yet been investigated.

There are several mentions of “upwind sources” in the discussion on page 9-46. Presumably, this refers to the San Francisco Bay Area, but it should be more clearly stated.

I found a couple of references that were missing or misdirected. All references should be checked for accuracy. The reference to McDade (2006) is not in the list of references (see line 14 on page 9-44). The reference for the comment on lines 6-9 of page 9-48 (Pitchford, et al., 2007) does not seem to be accurate. I could not find those statistics in that paper. I’m also skeptical of the statement on line 11 of page 9-50 that over half the sulfate in remote areas of the Pacific coastal sites is from outside the U.S. If this is a model result, it should be labeled as suspect.

The discussion of fine particles on page 9-84 should mention nanoparticle emissions as a direct source of fine particles. On page 9-87, “occult deposition” should be defined.

On page 9-88, the discussion of dry deposition should include mention of the surrogate surface work and sampler developed by Dr. Cliff Davidson of Carnegie-Mellon University.

I believe there is some redundancy in section 9.5.1.2, and possibly elsewhere in the document. I suspect this may be due to the number of authors required to produce such a comprehensive document. It may be possible to reduce its size by having a single person go through the entire document for consistency and to remove redundancy. This task may be too time-consuming to actually carry it out, though.

I will list a few detailed comments:

- On page 9-2 is the statement that nitrate important in most of California. It would be accurate to say “much of California”, but not “most”.
- Equation 9-2 needs work. It looks like it was copied unsuccessfully from another document. For example, “Large” is printed as “*L arg e*”. Also, the text refers to bold text but there is none.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

- There are grammatical errors throughout the chapter, but most of them are before section 9.3.5. For example, there are several uses of the word “dominate” that should be “dominant”. There are cases of misplaced parentheses and some minor typographical spelling errors. The chapter needs to be reviewed carefully for grammatical accuracy.

## **Comments from Mr. Ed Avol**

Review of PM ISA, First Draft (EPA 600/R-08/139, December 2008)

Ed Avol

(Initial comments, more forthcoming...)

### General Comments:

The First Draft ISA is a remarkable overview of the breadth of recent PM research conducted primarily in the United States over the past several years. EPA staff should collectively be congratulated and acknowledged for distilling an amazing array of data from multiple sources into one central location for consideration. The authors and reviewers listed as participating in the document's preparation are among the acknowledged experts in their respective fields, and EPA should be congratulated for assembling such a talented team to review this vast amount of material. There are, inevitably, differences of opinion in inferences, nuances, approaches, and conclusions, but the major accomplishment of assembling this material should not go unnoticed.

There are at least two comments/concerns I have with the stated approach. I was disappointed in the decision to minimize or dismiss extended consideration of ultra-fine particles or traffic-related pollution exhaust. The accumulating number of carefully-performed and peer-reviewed research describing the observed associations between fresh combustion exhaust (primarily from motor vehicles) and a range of health outcomes (respiratory, cardiovascular, birth-related, and even developmental) suggest that there is a rapidly accumulating body of information on which to objectively and seriously consider the need for a criteria standard. If this consideration does not move forward within the context of the periodic review of the current PM standards, I am concerned about what and where the EPA believes the appropriate venue to be. Other countries, most notably in the European Union, have moved forward in quantifying, monitoring, and regulating ultra-fine PM, while the United States has been slower to respond. In my opinion, this decision should be re-considered and re-opened for discussion.

I was also disappointed to see the decision to effectively restrict document consideration of health endpoints to primarily respiratory and cardiovascular results. Although the discussion "door" has arguably been left slightly ajar to allow some natal or pre-natal health outcomes to possibly stand in the proverbial doorway, the decision to not endorse and include these and other developmental outcomes as important and critical in our overall understanding of PM health effects seems outdated and short-sighted. Our responsibility to review the science and make recommendations that will lead to the development of standards that protect the public health extends to the full distribution of the population, and ought to include the widest breadth of available credible scientific information in those deliberations. Our understanding of the mechanisms and pathways of exposure and effect have evolved beyond limiting our

review to primary target organs of immediately present receptors, and our consideration of viable data for deliberations in standard-setting ought to, as well.

### Specific Comments, Chapter 3: Source to Human Exposure

P3-1, Introduction – There is a lot of discussion here (in the Introduction?) about soluble organic aerosols (SOAs), without adequate justification as to why or what other other key constituents might be present. In my opinion, this should be moved or at least prefaced by some transitional justification.

P3-1, lines 20-29, P3-2 lines 1-10 – move this to after SOA discussion in Section 3.3.

P3-2, lines 20-22 – “Within a street canyon,…” seems to be tacked on to this paragraph and out of place (no real connection to the paragraph, except only in the broadest possible sense).

P3-2, line 23 – “receptor modeling studies indicate that the main source…” sounds odd – isn’t receptor modeling focused on receptors?

P3-2, line 27 – Is the observation that “vegetative burning and traffic-related emissions were less consistently identified…”, both which would presumably be in smaller-than-PM<sub>2.5</sub> size ranges close to the source, really a surprise? PM<sub>2.5</sub> has a more regional spatial character.

P3-9, line 1 – It would be more accurate to begin this sentence “US national average…”

P3-23, line 10 – So what is the conclusion one is to draw from all of this?

P3-26, line 20 – There is LOTS of information presented on instrumentation and sampling; what to do with all of this to make it accessible? A summary table (such as the one in the Annex) would be helpful here, or reference to the annex table…

P3-26, line 21 – Why does this paragraph begin with this comment about “maximum concentration sites”? I would suggest that the paragraph begin with the sentence “...The AQS contains measurements…” in line 23, and the previous two sentences be reversed in order and moved to P3-27, line 2.

P3-27, lines 8-9 – Isn’t this description about neighborhood scale monitoring? How do air pollution episodes relate to micro <100m) or middle (100-500m) scales?

P3-27, line 15 – “Urban scale – This scale applies for assessment of air quality at an urban scale” is not much of an explanation…!

P3-27 – Reference is made to a number of different monitoring networks (NAMS, SLAMS, CSN, IMPROVE, NCORE,...) without ever explaining what they are or how they overlap or differ. How about a summary table showing the major networks, the frequency of sampling, typical monitoring array, sampling requirements, etc?

P3-28, line 4 – replace “built” with “located”

P3-28, line 21 – “...local conditions...” comment should be clarified; it refers to atmospheric or meteorology (temperature, humidity, pressure).

P3-33, Tables 3-5 to 3-10, include units in title (“...aged \_ years...”)

P3-38, line 12-13 – The comment is made here that there is a large amount of new information about ultra-fines...but then the decision is made to not consider it in the context of the PM review...seems a bit inconsistent.

P3-38, lines 27-28. While I don’t disagree with the Watson et al comment about spatial scales of interest, from a health standpoint, micro or middle scales (100s of meters) may be a critically important consideration (for example, in the context of proximity to busy roads).

P3-44, Table 3-12 – where was the 828 ug/m<sup>3</sup> 1 hour average reading observed, and what was its explanation?

P3-85, Figure 3-41 – It seems surprising that naphthalene, which typically is present in concentrations a magnitude higher than other PAHs, is in the bottom half of these plots...?

P3-90 – The layout of figures and text through this section is confusing to the reader, in that the text under a given figure does not describe or relate to that figure...can this be adjusted?

P3-92 – What is the purpose and utility of this “EPA region office” presentation of data? It is arguably a bit deceptive, since Region 9 (for example) shows a nice downward or flat trend in Figure 3-47 that is below the NAAQS line, but within that region [Southern California/Riverside] large areas are out of compliance and will remain so for several years to come (according the AQMP estimates by the local agency).

P3-94, Figure 3-49 – Here, too, the plots by EPA region office is deceptive. The trend lines look to be well under the NAAQS, but Southern California is still out of compliance. Are the most appropriate metrics being plotted and presented?

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

P3-132 – The discussion on this and the previous pages about temporal, spatial, and physical activity effects on exposure seems a little thin. There has been a LOT of work looking at personal exposures, time-activity, and spatial determinations (diary-based, for the most part, until recently). None of it, as it relates to PM exposure, is summarized or referenced here...?

P3-134, “New Developments in Microenvironmental Exposure Monitoring Techniques – I expected to see something about the NIH Exposure Biology Initiative samplers and innovations here (lab-on-a-chip, miniaturized samplers, etc) but no apparent mention...?”

P3-135, line 4 – replace “quiet” with “quiet”

P3-135, lines 4-10 – “Personal clouds”, variable locations, and other microenvironmental considerations may provide legitimate reasons for differences between personal measurements and fixed-site ambient measurements. The paragraph in the text makes it sound like the personal measurements are less credible or somehow fall short of being “equal” to a fixed-site monitor, when the true state of reality might very well be the reverse.

P3-138, lines 9-19 – Important points are raised in this section, but it should also be noted that one might infer from this discussion that zip codes are the appropriate unit for community assessment and assignment of exposure. This could be quite misleading in areas where the population is such that a given zip code covers a wide geographic, or variable topographic, or variable trafficked/road-coverage/vehicle-loaded, area. Accordingly, there should be some caveats or considerations associated with the document text.

P3-138, lines 20 and 22 – replace “among” with “between”

P3-147, line 13 – Is “0.3%” a printing error? This doesn’t seem like much to be concerned about...?

## Comments from Dr. Wayne Cascio

### Review of Draft Integrated Science Assessment (ISA)

Wayne Cascio, MD

March 25, 2009

#### Chapter 6

General comments: The authors, contributors, and reviewers of *Chapter 6: Integrated Health Effects of Short-Term PM Exposure of the ISA for Particulate Matter* have produced an comprehensive compendium of environmental health data that in large part achieves its goal of providing a thorough source of relevant human clinical and epidemiological data, and animal toxicological data along with an integrated and balanced discussion of its public health implications. This draft document appears to be unprecedented in scope and detail. In spite of the broad range of content and complexity the descriptions of the cited studies have an exceptional degree of accuracy and integration. The discussion is in general balanced, and the evidence supports the conclusions. The style of the *PM ISA* for is consistent and the document is easy to read and the concepts are clearly communicated.

In general the Tables and Figures of Chapter 6 are used effectively to communicate the copious information in a succinct manner. Annexes C, D and E are appropriate, adequate and effective in supporting the goals of the *PM ISA*.

The decision to include in Chapters 6 and 7 only toxicological inhalation and intratracheal instillation studies when conducted at PM concentrations  $<2 \text{ mg/m}^3$ , and *in vitro* studies when they contributed significantly to the understanding of health effects is logical because it is under these conditions that such studies provide the most support of biological plausibility for the health effects.

#### Specific Comments:

Figure 6-1. Excess risk estimates per  $10 \mu\text{g/m}^3$  increase in  $\text{PM}_{10}$ ,  $\text{PM}_{2.5}$ , and  $\text{PM}_{10-2.5}$  for studies of CVD ED visits and hospitalizations. Appropriate. The  $\text{PM}_{10-2.5}$  should read  $\text{PM}_{10-2.5}$ . The graphics of Figure 6-1 could be improved by placing the  $\text{PM}_{10}$ ,  $\text{PM}_{2.5}$ , and  $\text{PM}_{10-2.5}$  on the left hand side of Figure 6-1 in the same way as it is done in Table 6-6.

Figure 6-2; 6-3; 6-4. The graphics could be improved by placing the  $\text{PM}_{10}$ ,  $\text{PM}_{2.5}$ , and  $\text{PM}_{10-2.5}$  on the left hand side of Figure 6-2; 6-3; 6-4 in the same way as it is done in Table 6-6.

6-8, L. 3. ApoE<sup>-/-</sup> mice. This genetic model of atherosclerosis in the mouse is primarily a model of peripheral vascular disease rather than coronary artery disease. In the future other models should be incorporated into the atherosclerosis research, arrhythmia and cardiac dysfunction. Models that for example that modify the function of cells and proteins involved in the atherosclerotic process should be incorporated. Mouse models available today that might provide

more relevant information for coronary heart disease include the ApoE/LDL receptor double KO, the macrophage uPA-transgenic/apoE KO, SR-BI/apoE dKO, and the SR-BI/ApoE-R61<sup>h/h</sup>.

6-8, 6.2.1. Heart Rate Variability. The measures of heart rate variability (HRV) include time- and frequency-domain measures. The interpretation of HRV finding continues to be a challenge because studies judged to be well designed and with appropriate methods continue to show disparate findings. These unanticipated outcomes rather than explained by chance perhaps are indicating that the HRV result is reflecting a fundamental response of an individual that is determined in part by a number of factors including age and the presence of co-morbid conditions. It is also possible that time- and frequency-domain measure of HRV are inadequate to capture the true nature of PM's effect on heart rhythm. For example, no data contained in the previous AQCD or the current ISA describes any studies utilizing non-linear measures of HRV. Non-linear functions capture the structure and complexity of RR intervals and have the potential to provide a more detail of randomness of the RR dynamics and possibly be more prognostic.

6-16, L. 4. With respect to the paper by Gong et. al. 2003a, “This effect was observed immediately following the exposure and at 2-days post-exposure, ...”, it should read “.. and at 1 day post-exposure, ...”.

6-23, L. 13-25. The papers referenced regarding the assessment of arrhythmia by Dockery and colleagues (Dockery et al. 2005a, and 2005b were the first studies to investigate the association of air pollutants with arrhythmia utilizing an advanced internal cardiac defibrillator with the capability to store electrograms thereby allowing a qualified cardiologist to distinguish arrhythmia from artifact, and supraventricular from ventricular arrhythmia. This is an important point because such characterization was not present in the original paper by Peters et al. in 2000.

6-24, L. 11. “dame” should read “same”.

6-24, L. 12. “frome” should read “frame”.

6-27, L. 1-4. The following statement “Ectopic beats are defined as extra cardiac depolarizations and are the most common disturbance in heart rhythm. Ectopic beats are usually benign, and may present with or without symptoms, such as palpitations or dizziness. When three or more occur in succession, this is called a non-sustained ventricular tachycardia.” should be rewritten because of some inaccuracy. Consider the following, “Ectopic beats are defined as heart beats that originate at a location in the heart outside of the sinus node. They are the most common disturbance in heart rhythm. Ectopic beats are usually benign, and may present with or without symptoms, such as palpitations or dizziness. Such beats can arise in the atria or ventricles. When the origin is in the atria the beat is called an atrial or supraventricular ectopic beat. When such a beat occurs earlier than expected it is referred to as a premature supraventricular or atrial premature beat. Likewise, when the origin is in the ventricle the beat is defined as a ventricular ectopic beat, or when early a premature ventricular beat. When three or more occur ectopic beats occur in succession, this is called a non-sustained run of either supraventricular (atrial) or

ventricular origin. When the rate of the run is greater than 100 beats per minute it is defined as a tachycardia.”

6-29. L. 15. For completeness the following sentence, “... likely owing to their rapid heart rates (~600 and ~350 bpm, respectively).” should be amended to, “... likely owing to their rapid heart rates (~600 and ~350 bpm, respectively) and repolarizing currents.”.

6-29. L. 18-19. For accuracy the following phrase, “...ventricular depolarization elicits the QRS complex, and the biopotential recovery of the ventricles is reflected by the T-wave. “ should be amended to, “...ventricular depolarization elicits the QRS complex, and the T-wave represents the repolarization of the ventricles.”

6-33. 6.2.3.2. Human Clinical Studies. L. 21-26. Mills et al. (2007) assume that increased ST depression during exercise represents an increased magnitude of ischemia. This is a reasonable conclusion particularly in view of canine studies indicating that CAPS decreases coronary artery blood flow (Bartoli et al. 2008). Yet, it is not proven that the ST depression in man under conditions of PM exposure is caused by greater ischemia. An alternative interpretation is that the greater ST depression could be secondary to heterogeneity of electrophysiological effects of particulate exposure on the myocardium that is enhanced by the metabolic and ionic conditions associated with ischemia or increased heart rate.

6-36. L. 4. “bronchia” should read “bronchial”.

6-40. L. 8-16. Brauner et al. 2008 showed that eliminating particles with a HEPA filter in the homes of healthy aged adults improved microvascular function significantly. The effect was attributed to the removal of PM as gases were not impacted by the HEPA filter. These findings are similar to those observed in the California Freeway Study funded by the California Air Resource Board under the direction of Dr. William Hinds at UCLA School of Public Health where the filtering of PM from the passenger cab of a van containing research subjects riding on the 405 and 710 freeways in Los Angeles, California experienced fewer arrhythmias and a relative decrease in pro-NT BNP. These findings (Cascio et al. 2009) will be presented at American Thoracic Society in May 2009. Like Brauner et al. 2008 these outcomes were based on the elimination of PM rather than gases or the stress associated with being a passenger while traveling on the freeway.

6-52. L. 5-7. For clarity the “QA interval” can be used interchangeably with the term “systolic time interval”. The term “QA interval” appears throughout the text. For those less familiar with the terminology using the “QA interval” might be confusing. A reference might be helpful as well. For example, Cambridge D and Whiting MV. Evaluation of the QA interval as an index of cardiac contractility in anaesthetized dogs: responses to changes in cardiac loading and heart rate. Cardiovascular Res. 1986: 444-50, would provide the basis for this measurement.

6-49. L. 7-16. Wellenius et al. 2007 reported that in a group of subjects with LV dysfunction that

PM did not affect measurements of BNP, failing to prove the hypothesis that PM can worsen LV function. Yet, BNP the active peptide has a very short half-life and might not be the best biomarker for such a study. NT-pro BNP, the inactive peptide also responsive to LV ventricular pressure but with a substantially longer half-life might have been a better biomarker to assess transient changes in LV function associated with PM and other air pollutants. Thus the absence of a correlation between PM and BNP does not prove that PM does not have an impact on RV or LV function in individuals with impaired cardiac mechanics.

6-59. Section 6.2.8. “Blood Coagulation” is more appropriately named “Hemostasis, Thrombosis and Coagulation Factors”.

6-97. L. 15-7. Just published in *Environmental Health Perspectives* are the findings of a CAPS coarse particle study. The reference is Graff DW, Cascio WE, Pappold A, Zhu H, Huang Y-C T, Devlin RB. Exposure to concentrated coarse air pollution particles causes mild cardiopulmonary effects in healthy young adults. EHP doi: 10.1289/ehp.0900558. Available 23 March 2009. In this study 14 healthy young volunteers were exposed to coarse concentrated ambient particles (CAPS) and filtered air. Coarse Particle concentration averaged 89.0 µg/m<sup>3</sup> (range was 23.7 – 159.6). Volunteers were exposed to coarse CAPS and filtered air for two hours while undergoing intermittent exercise in a single-blind, cross-over study. Pulmonary, cardiac, and hematological endpoints were measured before exposure, immediately after exposure, and again 24 hours after exposure. Compared to filtered air exposure, coarse CAPS exposure produced mild pulmonary inflammation as evidenced by a small increase in polymorphonuclear neutrophils (PMNs) in the bronchoalveolar lavage (BAL) fluid 20 hours post-exposure. Changes in pulmonary function were not observed. Blood tissue plasminogen activator (tPA) was decreased 20 hours after exposure. SDNN, a measure of overall HRV was decreased 20 hours after exposure to CAPS. Consequently it is concluded that coarse CAPS exposure induces a mild physiologic response in healthy young volunteers approximately 20 hours after exposure. These changes are similar in type and magnitude to changes reported previously for healthy volunteers exposed to fine CAPS, suggesting that both size fractions are comparable at inducing acute cardiopulmonary changes.

6-99. L. 10. “PM<sub>2</sub>” Should read “PM<sub>2.5</sub>”.

6-100. L. 21 and 23. “H” should read either “HR” or “heart rate”.

6-101, L. 29. “... organic and EC fraction..” should be written either as “...organic and elemental carbon...”, or “OC and EC”.

6-106, L. 22. “H” should read “heart rate”.

6-107, L. 23-24. “There is one study that used an indirect measure of cardiac contractility (QA-interval) during ultrafine CAPs...” should be written as, “There is one study that used an indirect measure of cardiac contractility, the systolic time interval, as assessed by the QA-interval during ultrafine CAPs...”.

6-125, L. 30-32., and 6-126, L.1. “Pietropaoli et al. (2004) observed a significant reduction in MMEF and DLCO in healthy adults 21 hours after a 2-h exposure to ultrafine carbon particles (50 µg/m<sup>3</sup>). This reduction in DLCO may reflect a PM-induced vasoconstrictive effect on the pulmonary vasculature.” This observation might be important to the observation in the California Freeway Study (Cascio et al. accepted for presentation at ATS May 2009) in which exposure to traffic related particles produced a relative increase in arrhythmia and NT-proBNP compared to filtered air. The release of NT-proBNP is consistent with an acute increase in pulmonary pressures due to pulmonary vasoconstriction with attendant RV stress.

6-134, L. 13. “Differenc<sup>t</sup>” should be written “Differences”.

6-142, L. 25-26. Write out, “fine+ultrafine”.

6-6-150, L. 10 . “patter” should read “pattern”.

6-197, L. 22. “domaminergic” should be written as “dopaminergic”.

6-198, 6.4.3. Summary and Causal Determination. It is agreed that the weight of the evidence is inadequate to assign a causal relationship between PM<sub>10</sub>, PM<sub>2.5</sub>, PM<sub>10-2.5</sub>, ultrafine particles, or specific PM components to CNS outcomes. Yet, this data is some of the most intriguing. These early findings should stimulate more comprehensive studies to elucidate mechanism in the animal models and man.

6-240, L. 16. “causes-specifici” should be written, “cause-specific”.

6-243, L.11. “HAs” should be written out as, “hospital admissions”.

## **Chapter 7.**

The conclusions related to causation are conservative and supported by the evidence.

7-2, L. 17-19. The statement, “The advanced lesion that develops from this process can occlude perfusion to distal tissue, causing ischemia, and erode, degrade, or even rupture, revealing coagulant initiators (tissue factor) that cause major clotting disorders and infarction or stroke.” Should be clarified. Consider the following, “The advanced lesion that develops from this process can occlude perfusion to distal tissue, causing ischemia, and erode, degrade, or even rupture, revealing initiators of thrombosis (tissue factor) that cause major disorders caused by arterial thrombosis and thromboembolism such as coronary artery syndrome or stroke.”

7-3, L. 8. The statement, “Agatston scores are frequently used to classify individuals into one of five groups (zero; mild; moderate; severe; extensive) or according to age- and sex-specific

percentiles of the CAC distribution (Erbel et al., 2007).” Should be amended to read, “...the CAC distribution (Erbel et al., 2007) and as such the greatest utility of the Agatston score is in ascribing a long-term clinical risk for cardiac events. Yet, the Agatston score is not sensitive to low levels of vascular calcium and as such this insensitivity might limit its utility in longitudinal epidemiological studies.”

7-3, L. 9-20. Carotid artery internal medial thickness is an established measurement of large vessel atherosclerosis. Yet, recent clinical trials have raised the issue of its suitability as a measure of progression of atherosclerosis. As recent study puts this issue into perspective. (Doggan S, Plantinga Y, Evans GW, Meijer R, Grobbee DE, Cots MS, Opal Investigators. Ultrasound protocols to measure carotid intima-media thickness: a post-hoc analysis of the OPAL study. *Curr Med Res Opin* 2009; 25(1):109-22.). In their study they showed that in “healthy middle-aged subjects mean common CIMT protocols that include measurements at both near and far walls at multiple (> or = 2) angles provide highest reproducibility combined with largest estimates of CIMT progression measured with high precision...” Such approaches are generally not taken this most likely limits the sensitivity of the assay.

7-4, L. 3-14. As discussed previously the Agatston scale is expected to be insensitive to small changes in vascular wall calcium.

7-84, L. 27. The font of “infant mortality” should be changed to match the text.

7-86, L. 4. The “n” should be written out as “numbers of subjects”.

## **Chapter 8.**

Comment: The C-R relationship focuses on mortality effects with short- and long-term exposure to PM. The mortality endpoint is a hard endpoint but is also less sensitive indicator of health effects attendant to PM. Hospitalizations for clinical conditions are likely to provide greater sensitivity in determining the C-R relationship. From a public health perspective having a more sensitive indicator will be important to fully understanding the potential health impact of PM, particularly at low concentrations. Yet, such data is limited and not sufficient to establish firm conclusions. More data is needed in this area.

The definitions of susceptibility and vulnerability are logical and functional. Such definitions can be effectively used to categorize and summarize clinical studies with similar characteristics.

Pg. 8-6. L. 2. Spelling. “Medixare” should read “Medicare”.

## **References**

R-3. The full citation is now available: Andersen, Z. J., P. Wahlin, et al. (2008). "Size distribution and total number concentration of ultrafine and accumulation mode particles and

hospital admissions in children and the elderly in Copenhagen, Denmark." Occup Environ Med 65(7): 458-66.

R-7. Full reference now available. Bell, M. L., K. Ebisu, et al. (2008). "Seasonal and regional short-term effects of fine particles on hospital admissions in 202 US counties, 1999-2005." Am J Epidemiol 168(11): 1301-10.

### **New References of Relevance not included in *PM ISA* and their Abstracts**

**Carder, M., R. McNamee, et al. (2008). "Interacting effects of particulate pollution and cold temperature on cardiorespiratory mortality in Scotland." Occup Environ Med 65(3): 197-204.** To determine whether the effect of black smoke on cardiorespiratory mortality is modified by cold temperatures. METHODS: Poisson regression models were used to investigate the relationship between lagged black smoke concentration and daily mortality, and whether the effect of black smoke on mortality was modified by cold temperature for three Scottish cities from January 1981 to December 2001. MAIN RESULTS: For all-cause respiratory and non-cardiorespiratory mortality, there was a significant association between mortality and lagged black smoke concentration. Generally the maximum black smoke effect occurred at lag 0, although these estimates were not statistically significant. A 10 mugm(-3) increase in the daily mean black smoke concentration on any given day was associated with a 1.68% (95% CI 0.72 to 2.65) increase in all-cause mortality and a 0.43% (95% CI -0.97 to 1.86), 5.36% (95% CI 2.93 to 7.84) and 2.13% (95% CI 0.82 to 3.47) increase in cardiovascular, respiratory and non-cardiorespiratory mortality, respectively, over the ensuing 30-day period. The effect of black smoke on mortality did not vary significantly between seasons (cool and warm periods). For all-cause, cardiovascular and non-cardiorespiratory mortality the inclusion of interaction terms did not improve the models, although for all-cause and non-cardiorespiratory mortality there was a suggestion for interaction between temperature and recent black smoke exposure. The results of this study suggested a greater effect of black smoke on mortality at low temperatures. Since extremes of cold and particulate pollution may coexist, for example during temperature inversion, these results may have important public health implications.

**Franco Suglia, S., A. Gryparis, et al. (2008). "Association between traffic-related black carbon exposure and lung function among urban women." Environ Health Perspect 116(10): 1333-7.** BACKGROUND: Although a number of studies have documented the relationship between lung function and traffic-related pollution among children, few have focused on adult lung function or examined community-based populations. OBJECTIVE: We examined the relationship between black carbon (BC), a surrogate of traffic-related particles, and lung function among women in the Maternal-Infant Smoking Study of East Boston, an urban cohort in Boston, Massachusetts. METHODS: We estimated local BC levels using a validated spatiotemporal land-use regression model, derived using ambient and indoor monitor data. We examined associations between percent predicted pulmonary function and predicted BC using linear regression, adjusting for sociodemographics (individual and neighborhood levels),

smoking status, occupational exposure, type of cooking fuel, and a diagnosis of asthma or chronic bronchitis. RESULTS: The sample of 272 women 18-42 years of age included 57% who self-identified as Hispanic versus 43% white, and 18% who were current smokers. Mean +/- SD predicted annual BC exposure level was 0.62 +/- 0.2 microg/m<sup>3</sup>. In adjusted analysis, BC (per interquartile range increase) was associated with a 1.1% decrease [95% confidence interval (CI), -2.5% to 0.3%] in forced expiratory volume in 1 sec, a 0.6% decrease (95% CI, -1.9% to 0.6%) in forced vital capacity, and a 3.0% decrease (95% CI, -5.8% to -0.2%) in forced mid-expiratory flow rate. We noted differential effects by smoking status in that former smokers were most affected by BC exposure, whereas current smokers were not affected. CONCLUSION: In this cohort, exposure to traffic-related BC, a component of particulate matter, independently predicted decreased lung function in urban women, when adjusting for tobacco smoke, asthma diagnosis, and socioeconomic status.

**Goldberg, M. S., N. Giannetti, et al. (2008). "A panel study in congestive heart failure to estimate the short-term effects from personal factors and environmental conditions on oxygen saturation and pulse rate." Occup Environ Med 65(10): 659-66.** This daily diary panel study in Montreal, Quebec, was carried out to determine whether oxygen saturation and pulse rate were associated with selected personal factors, weather conditions and air pollution. Thirty-one subjects with CHF participated in this study in 2002 and 2003. Over a 2-month period, the investigators measured their oxygen saturation, pulse rate, weight and temperature each morning and recorded these and other data in a daily diary. Air pollution and weather conditions were obtained from fixed-site monitoring stations. The study made use of mixed regression models, adjusting for within-subject serial correlation and temporal trends, to determine the association between oxygen saturation and pulse rate and personal and environmental variables. Depending on the model, we accounted for the effects of a variety of personal variables (e.g., body temperature, salt consumption) as well as nitrogen dioxide (NO<sub>2</sub>), ozone, maximum temperature and change in barometric pressure at 8:00 from the previous day. RESULTS: In multivariable analyses, the study found that oxygen saturation was reduced when subjects reported that they were ill, consumed salt, or drank liquids on the previous day and had higher body temperatures on the concurrent day (only the latter was statistically significant). Relative humidity and decreased atmospheric pressure from the previous day were associated with oxygen saturation. In univariate analyses, there was negative associations with concentrations of fine particulates, ozone, and sulphur dioxide (SO<sub>2</sub>), but only SO<sub>2</sub> was significant after adjustment for the effects of weather. For pulse rate, no associations were found for the personal variables and in univariate analyses the study found positive associations with NO<sub>2</sub>, fine particulates (aerodynamic diameter of 2.5 microm or under, PM<sub>2.5</sub>), SO<sub>2</sub>, and maximum temperature, although only the latter two were significant after adjustment for environmental effects. The findings from the present investigation suggest that personal and environmental conditions affect intermediate physiological parameters that may affect the health of CHF patients.

**Liao, D., E. A. Whitsel, et al. (2009). "Ambient particulate air pollution and ectopy--the environmental epidemiology of arrhythmogenesis in Women's Health Initiative Study,**

**1999-2004." J Toxicol Environ Health A 72(1): 30-8.** The relationships between ambient PM(2.5) and PM(10) and arrhythmia and the effect modification by cigarette smoking were investigated. Data from U.S. Environmental Protection Agency (EPA) air quality monitors and an established national-scale, log-normal kriging method were used to spatially estimate daily mean concentrations of PM at addresses of 57,422 individuals from 59 examination sites in 24 U.S. states in 1999-2004. The acute and subacute exposures were estimated as mean, geocoded address-specific PM concentrations on the day of, 0-2 d before, and averaged over 30 d before the electrocardiogram (ECG) (Lag(0); Lag(1); Lag(2); Lag(1-30)). At the time of standard 12-lead resting ECG, the mean age (SD) of participants was 67.5 (6.9) yr (84% non-Hispanic White; 6% current smoker; 15% with coronary heart disease; 5% with ectopy). After the identification of significant effect modifiers, two-stage random-effects models were used to calculate center-pooled odds ratios and 95% confidence intervals (OR, 95% CI) of arrhythmia per 10 mug/m(3) increase in PM concentrations. Among current smokers, Lag(0) and Lag(1) PM concentrations were significantly associated ventricular ectopy (VE)-the OR (95% CI) for VE among current smokers was 2 (1.32-3.3) and 1.32 (1.07-1.65) at Lag(1) PM(2.5) and PM(10), respectively. The interactions between current smoking and acute exposures (Lag(0); Lag(1); Lag(2)) were significant in relationship to VE. Acute exposures were not significantly associated with supraventricular ectopy (SVE), or with VE among nonsmokers. Subacute (Lag(1-30)) exposures were not significantly associated with arrhythmia. Acute PM(2.5) and PM(10) exposure is directly associated with the odds of VE among smokers, suggesting that they are more vulnerable to the arrhythmogenic effects of PM.

Ljungman, P. L., N. Berglind, et al. (2008). "Rapid effects of air pollution on ventricular arrhythmias." Eur Heart J 29(23): 2894-901. Air pollution has been associated with ventricular arrhythmias in patients with implantable cardioverter defibrillators (ICDs) for exposure periods of 24-48 h. Only two studies have investigated exposure periods <24 h. We aimed to explore such effects during the 2 and 24 preceding hours as well as in relation to distance from the place of the event to the air pollution monitor. METHODS AND RESULTS: We used a case-crossover design to investigate the effects of particulate matter <10 microm in diameter (PM10) and nitrogen dioxide (NO2) in 211 patients with ICD devices in Gothenburg and Stockholm, Sweden. Events interpreted as ventricular arrhythmias were downloaded from the ICDs, and air pollution data were collected from urban background monitors. We found an association between 2 h moving averages of PM10 and ventricular arrhythmia [odds ratio (OR) 1.31, 95% confidence interval (CI) 1.00-1.72], whereas the OR for 24 h moving averages was 1.24 (95% CI 0.87-1.76). Corresponding ORs for events occurring closest to the air pollution monitor were 1.76 (95% CI 1.18-2.61) and 1.74 (95% CI 1.07-2.84), respectively. Events occurring in Gothenburg showed stronger associations than in Stockholm. CONCLUSION: Moderate increases in air pollution appear to be associated with ventricular arrhythmias in ICD patients already after 2 h, although future studies including larger numbers of events are required to confirm these findings. Representative geographical exposure classification seems important in studies of these effects.

**Lucking, A. J., M. Lundback, et al. (2008). "Diesel exhaust inhalation increases thrombus**

**formation in man." Eur Heart J 29(24): 3043-51.** Although the mechanism is unclear, exposure to traffic-derived air pollution is a trigger for acute myocardial infarction (MI). The aim of this study is to investigate the effect of diesel exhaust inhalation on platelet activation and thrombus formation in men. **METHODS AND RESULTS:** In a double-blind randomized crossover study, 20 healthy volunteers were exposed to dilute diesel exhaust (350 microg/m<sup>3</sup>) and filtered air. Thrombus formation, coagulation, platelet activation, and inflammatory markers were measured at 2 and 6 h following exposure. Thrombus formation was measured using the Badimon ex vivo perfusion chamber. Platelet activation was assessed by flow cytometry. Compared with filtered air, diesel exhaust inhalation increased thrombus formation under low- and high-shear conditions by 24% [change in thrombus area 2229 microm<sup>2</sup>, 95% confidence interval (CI) 1143-3315 microm<sup>2</sup>, P = 0.0002] and 19% (change in thrombus area 2451 microm<sup>2</sup>, 95% CI 1190-3712 microm<sup>2</sup>, P = 0.0005), respectively. This increased thrombogenicity was seen at 2 and 6 h, using two different diesel engines and fuels. Diesel exhaust also increased platelet-neutrophil and platelet-monocyte aggregates by 52% (absolute change 6%, 95% CI 2-10%, P = 0.01) and 30% (absolute change 3%, 95% CI 0.2-7%, P = 0.03), respectively, at 2 h following exposure compared with filtered air. **CONCLUSION:** Inhalation of diesel exhaust increases ex vivo thrombus formation and causes in vivo platelet activation in man. These findings provide a potential mechanism linking exposure to combustion-derived air pollution with the triggering of acute MI.

**Pereira Filho, M. A., L. A. Pereira, et al. (2008). "Effect of air pollution on diabetes and cardiovascular diseases in Sao Paulo, Brazil." Braz J Med Biol Res 41(6): 526-32.** Type 2 diabetes increases the risk of cardiovascular mortality and these patients, even without previous myocardial infarction, run the risk of fatal coronary heart disease similar to non-diabetic patients surviving myocardial infarction. There is evidence showing that particulate matter air pollution is associated with increases in cardiopulmonary morbidity and mortality. The present study was carried out to evaluate the effect of diabetes mellitus on the association of air pollution with cardiovascular emergency room visits in a tertiary referral hospital in the city of Sao Paulo. Using a time-series approach, and adopting generalized linear Poisson regression models, we assessed the effect of daily variations in PM<sub>10</sub>, CO, NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub> on the daily number of emergency room visits for cardiovascular diseases in diabetic and non-diabetic patients from 2001 to 2003. A semi-parametric smoother (natural spline) was adopted to control long-term trends, linear term seasonal usage and weather variables. In this period, 45,000 cardiovascular emergency room visits were registered. The observed increase in interquartile range within the 2-day moving average of 8.0 microg/m<sup>3</sup> SO<sub>2</sub> was associated with 7.0% (95%CI: 4.0-11.0) and 20.0% (95%CI: 5.0-44.0) increases in cardiovascular disease emergency room visits by non-diabetic and diabetic groups, respectively. These data indicate that air pollution causes an increase of cardiovascular emergency room visits, and that diabetic patients are extremely susceptible to the adverse effects of air pollution on their health conditions.

**Pope, C. A., 3rd, D. G. Renlund, et al. (2008). "Relation of heart failure hospitalization to exposure to fine particulate air pollution." Am J Cardiol 102(9): 1230-4.** Cardiopulmonary disease has been associated with particulate matter (PM) air pollution. There is evidence that

exposure to elevated PM concentrations increases risk of acute ischemic heart disease events, alters cardiac autonomic function, and increases risk of arrhythmias. It is plausible, therefore, that PM exposure may exacerbate heart failure (HF). A case-crossover study design was used to explore associations between fine PM (PM<sub>2.5</sub>): particles with an aerodynamic diameter  $\leq$  2.5 microm) and 2,628 HF hospitalizations. Patients lived on Utah's Wasatch Front and were drawn from those hospitalized at Intermountain Healthcare facilities with a primary diagnosis of HF. A 14-day lagged cumulative moving average of 10 microg/m<sup>3</sup> PM<sub>2.5</sub> was associated with a 13.1% (95% confidence interval 1.3 to 26.2) increase in HF admissions. The strongest PM<sub>2.5</sub>-HF associations were for elderly patients who had previously been admitted for HF and who required only a short period of hospitalization. HF hospitalizations are associated with lagged cumulative exposure to PM<sub>2.5</sub> of approximately 2 weeks. In conclusion, particulate air pollution may play a role in precipitating acute cardiac decompensation in otherwise well-managed patients with HF, perhaps through effects of PM on myocardial ischemia, cardiac autonomic function, and/or arrhythmic effects.

**Rundell, K. W. and R. Caviston (2008). "Ultrafine and fine particulate matter inhalation decreases exercise performance in healthy subjects." J Strength Cond Res 22(1): 2-5.** The purpose of this study was to investigate effects of PM<sub>1</sub> (particulate matter with aerodynamic diameter 0.02-2 microm) inhalation on exercise performance in healthy subjects. Inhalation of internal combustion-derived PM is associated with adverse effects to the pulmonary and muscle microcirculation. No data are available concerning air pollution and exercise performance. Fifteen healthy college-aged males performed 4 maximal effort 6-min cycle ergometer trials while breathing low or high PM<sub>1</sub> to achieve maximal work accumulation (kJ). Low PM<sub>1</sub> inhalation trials 1 and 2 were separated by 3 days; then after a 7 day washout, trials 3 and 4 (separated by 3 days) were done while breathing high PM<sub>1</sub> generated from a gasoline engine; CO was kept below 10 ppm. Lung function was done after trial 1 to verify nonasthmatic status. Lung function was normal before and after low PM<sub>1</sub> exercise. PM<sub>1</sub> number counts were not different between high PM<sub>1</sub> trials (336,730 +/- 149,206 and 396,200 +/- 82,564 for trial 3 and 4, respectively) and were different from low PM<sub>1</sub> trial number counts (2,260 +/- 500) ( $P < 0.0001$ ). Mean heart rate was not different between trials (189 +/- 6.0, 188 +/- 7.6, 188 +/- 7.6, 187 +/- 7.4, for low and high PM<sub>1</sub> trials; respectively). Work accumulated was not different between low PM<sub>1</sub> trials (96.1 +/- 9.38 versus 96.6 +/- 10.83 kJ) and the first high PM<sub>1</sub> trial (trial 3, 96.8 +/- 10.65 kJ). Work accumulated in the second high PM<sub>1</sub> trial 4, 91.3 +/- 10.04 kJ) was less than in low PM<sub>1</sub> trials 1 and 2, and high PM<sub>1</sub> trial 3 ( $P = 0.004$ ,  $P = 0.003$ ,  $P = 0.0008$ ; respectively). Acute inhalation of high (PM<sub>1</sub>) typical of many urban environments could impair exercise performance.

**Sint, T., J. F. Donohue, et al. (2008). "Ambient air pollution particles and the acute exacerbation of chronic obstructive pulmonary disease." Inhal Toxicol 20(1): 25-9.** Investigation has repeatedly demonstrated an association between exposure to ambient air pollution particles and numerous indices of human morbidity and mortality. Individuals with chronic obstructive pulmonary disease (COPD) are among those with an increased sensitivity to air pollution particles. Current and ex-smokers account for 80 to 85% of all those with COPD.

The human breathing in an urban site with a significant level of particulate matter (PM) may be exposed to 720 microg daily. A single cigarette introduces 15,000 to 40,000 microg particle into the respiratory tract of the smoker. It is subsequently confounding why such a relatively small mass of airborne PM should have any biological effect in the patient with COPD, as these individuals are repeatedly exposed to particles (with a similar size and composition) at perhaps a thousandfold the mass of ambient PM. Regarding this increased sensitivity of COPD patients to air pollution particles, there are several possible explanations for this seeming contradiction, including correlations of PM levels with other components of air pollution, an accumulation of multiple independent risk factors in a patient, changes in individual activity patterns, disparities in dosimetry between healthy subjects and COPD patients, and some unique characteristic of an ambient air pollution PM. Regardless of the underlying mechanism for the increased sensitivity of COPD patients, exposures of these individuals to elevated levels of PM should be discouraged. To provide a greater awareness of PM levels, the U.S. Environmental Protection Agency now includes levels of air pollution particles in an air quality index.

**Rhoden, C. R., E. Ghelfi, et al. (2008). "Pulmonary inflammation by ambient air particles is mediated by superoxide anion." Inhal Toxicol 20(1): 11-5.** Lung inflammation is a key response to increased levels of particulate air pollution (PM); however, the cellular mechanisms leading to this response remain poorly understood. We have previously shown that oxidants are critical mediators of the inflammatory response elicited by inhalation of ambient air particles. Here we tested the possible role of a specific oxidant, superoxide anion, by using the membrane-permeable analog of superoxide dismutase, Mn(III) tetrakis(4-benzoic acid)porphyrin chloride (MnTBAP). Adult Sprague-Dawley rats were instilled with either urban air particles (UAP) or saline. MnTBAP-treated rats received 10 mg/kg (ip) MnTBAP 2 h prior to exposure to UAP. Recruitment of inflammatory cells into bronchoalveolar lavage was evaluated 4 h after instillation. Rats exposed to UAP showed significant increases in the total cell number ( $8.9 \pm 0.6 \times 10^6$ ; sham:  $5.1 \pm 0.6 \times 10^6$ ,  $p < .02$ ), the numbers of polymorphonuclear leukocytes ( $26 \pm 4\%$ ; sham:  $6 \pm 1\%$ ,  $p < .0001$ ), protein levels ( $1.2 \pm 0.5$  mg/ml, sham:  $0.4 \pm 0.1$  mg/ml,  $p < .001$ ), and a trend of increase in myeloperoxidase levels ( $5 \pm 1$ ; sham:  $2 \pm 1$  mU/ml) in bronchoalveolar lavage (BAL). Pretreatment with MnTBAP at a dose that prevented UAP-induced increases in oxidants effectively prevented increase in BAL cells ( $2.7 \pm 0.6 \times 10^6$ ,  $p < .0001$  vs. UAP), PMN influx into the lungs ( $4 \pm 3\%$ ,  $p < .0001$  vs. UAP), and increase in myeloperoxidase ( $2 \pm 1$  mU/ml) and protein levels in BAL ( $0.1 \pm 0.1$  mg/ml). These data indicate that superoxide anion is a critical mediator of the inflammatory response elicited by PM deposition in the lung.

**Yatera, K., J. Hsieh, et al. (2008). "Particulate matter air pollution exposure promotes recruitment of monocytes into atherosclerotic plaques." Am J Physiol Heart Circ Physiol 294(2): H944-53.** Epidemiologic studies have shown an association between exposure to ambient particulate air pollution  $<10$  microm in diameter (PM(10)) and increased cardiovascular morbidity and mortality. We previously showed that PM(10) exposure causes progression of atherosclerosis in coronary arteries. We postulate that the recruitment of monocytes from the circulation into atherosclerotic lesions is a key step in this PM(10)-induced acceleration of

atherosclerosis. The study objective was to quantify the recruitment of circulating monocytes into vessel walls and the progression of atherosclerotic plaques induced by exposure to PM(10). Female Watanabe heritable hyperlipidemic rabbits, which naturally develop systemic atherosclerosis, were exposed to PM(10) (EHC-93) or vehicle by intratracheal instillation twice a week for 4 wk. Monocytes, labeled with 5-bromo-2'-deoxyuridine (BrdU) in donors, were transfused to recipient rabbits as whole blood, and the recruitment of BrdU-labeled cells into vessel walls and plaques in recipients was measured by quantitative histological methodology. Exposure to PM(10) caused progression of atherosclerotic lesions in thoracic and abdominal aorta. It also decreased circulating monocyte counts, decreased circulating monocytes expressing high levels of CD31 (platelet endothelial cell adhesion molecule-1) and CD49d (very late antigen-4 alpha-chain), and increased expression of CD54 (ICAM-1) and CD106 (VCAM-1) in plaques. Exposure to PM(10) increased the number of BrdU-labeled monocytes adherent to endothelium over plaques and increased the migration of BrdU-labeled monocytes into plaques and smooth muscle underneath plaques. We conclude that exposure to ambient air pollution particles promotes the recruitment of circulating monocytes into atherosclerotic plaques and speculate that this is a critically important step in the PM(10)-induced progression of atherosclerosis.

**Baccarelli, A., P. A. Cassano, et al. (2008). "Cardiac autonomic dysfunction: effects from particulate air pollution and protection by dietary methyl nutrients and metabolic polymorphisms." Circulation 117(14): 1802-9.** Particulate air pollution is associated with cardiovascular mortality and morbidity. To help identify mechanisms of action and protective/susceptibility factors, we evaluated whether the effect of particulate matter <2.5 µm in aerodynamic diameter (PM(2.5)) on heart rate variability was modified by dietary intakes of methyl nutrients (folate, vitamins B(6) and B(12), methionine) and related gene polymorphisms (C677T methylenetetrahydrofolate reductase [MTHFR] and C1420T cytoplasmic serine hydroxymethyltransferase [cSHMT]). **METHODS AND RESULTS:** Heart rate variability and dietary data were obtained between 2000 and 2005 from 549 elderly men from the Normative Aging Study. In carriers of [CT/TT] MTHFR genotypes, the SD of normal-to-normal intervals was 17.1% (95% CI, 6.5 to 26.4; P=0.002) lower than in CC MTHFR subjects. In the same [CT/TT] MTHFR subjects, each 10-µg/m<sup>3</sup> increase in PM(2.5) in the 48 hours before the examination was associated with a further 8.8% (95% CI, 0.2 to 16.7; P=0.047) decrease in the SDNN. In [CC] cSHMT carriers, PM(2.5) was associated with an 11.8% (95% CI, 1.8 to 20.8; P=0.02) decrease in SDNN. No PM(2.5)-SDNN association was found in subjects with either [CC] MTHFR or [CT/TT] cSHMT genotypes. The negative effects of PM(2.5) were abrogated in subjects with higher intakes (above median levels) of B(6), B(12), or methionine. PM(2.5) was negatively associated with heart rate variability in subjects with lower intakes, but no PM(2.5) effect was found in the higher intake groups. **CONCLUSIONS:** Genetic and nutritional variations in the methionine cycle affect heart rate variability either independently or by modifying the effects of PM2.5.

**Gallus, S., E. Negri, et al. (2008). "European studies on long-term exposure to ambient particulate matter and lung cancer." Eur J Cancer Prev 17(3): 191-4.** European

epidemiological studies on ambient air pollution and cancer published before December 2006 are reviewed, with focus on five analytic studies providing data on the association between various measures of particulate matter (PM) and lung cancer. A case-control study of 755 men who died from lung cancer in Trieste, Italy, reported that, compared with less than 0.18 g/m/day of deposition of particulate, the relative risk (RR) was 1.1 [95% confidence interval (CI): 0.8-1.5] for 0.18-0.30 and 1.4 (95% CI: 1.1-1.8) for more than 0.30 g/m/day. In the Netherlands Cohort Study on Diet and Cancer with 60 deaths from lung cancer, the RR was 1.06 (95% CI: 0.43-2.63) for an increase of 10 mug/m in black smoke. In the French Pollution Atmosphérique et Affections Respiratoires Chroniques study cohort based on 178 deaths from lung cancer, the RR associated with an increase in exposure to 10 mug/m of total suspended particulate was 0.97 (95% CI: 0.94-1.01). A nested case-control study within the European Prospective Investigation on Cancer and Nutrition included 113 nonsmokers or exsmokers diagnosed with lung cancer and 312 controls. The RRs were 0.91 (95% CI: 0.70-1.18) for an increase in PM with diameter  $\leq 10$   $\mu\text{m}$  (PM<sub>10</sub>) of 10 mug/m, and 0.98 (95% CI: 0.66-1.45) for exposure over 27 mug/m compared with less than 27 mug/m. In a Norwegian record linkage study, based on 1453 lung cancer deaths, no significant excess risk was found for men, and a modest association was observed for women. European studies of PM exposure and lung cancer do not show a clear association, but uncertainties remain for the measurement of exposure and latency.

**Jerrett, M., R. T. Burnett, et al. (2009). "Long-term ozone exposure and mortality." N Engl J Med 360(11): 1085-95.** Although many studies have linked elevations in tropospheric ozone to adverse health outcomes, the effect of long-term exposure to ozone on air pollution-related mortality remains uncertain. We examined the potential contribution of exposure to ozone to the risk of death from cardiopulmonary causes and specifically to death from respiratory causes. METHODS: Data from the study cohort of the American Cancer Society Cancer Prevention Study II were correlated with air-pollution data from 96 metropolitan statistical areas in the United States. Data were analyzed from 448,850 subjects, with 118,777 deaths in an 18-year follow-up period. Data on daily maximum ozone concentrations were obtained from April 1 to September 30 for the years 1977 through 2000. Data on concentrations of fine particulate matter (particles that are  $\leq 2.5$  microm in aerodynamic diameter [PM(2.5)]) were obtained for the years 1999 and 2000. Associations between ozone concentrations and the risk of death were evaluated with the use of standard and multilevel Cox regression models. RESULTS: In single-pollutant models, increased concentrations of either PM(2.5) or ozone were significantly associated with an increased risk of death from cardiopulmonary causes. In two-pollutant models, PM(2.5) was associated with the risk of death from cardiovascular causes, whereas ozone was associated with the risk of death from respiratory causes. The estimated relative risk of death from respiratory causes that was associated with an increment in ozone concentration of 10 ppb was 1.040 (95% confidence interval, 1.010 to 1.067). The association of ozone with the risk of death from respiratory causes was insensitive to adjustment for confounders and to the type of statistical model used. CONCLUSIONS: In this large study, we were not able to detect an effect of ozone on the risk of death from cardiovascular causes when the concentration of PM(2.5) was taken into account. We did, however, demonstrate a significant increase in the risk of death from respiratory causes in association with an increase in ozone concentration.

**Pope, C. A., 3rd, M. Ezzati, et al. (2009). "Fine-particulate air pollution and life expectancy in the United States." N Engl J Med 360(4): 376-86.** Exposure to fine-particulate air pollution has been associated with increased morbidity and mortality, suggesting that sustained reductions in pollution exposure should result in improved life expectancy. This study directly evaluated the changes in life expectancy associated with differential changes in fine particulate air pollution that occurred in the United States during the 1980s and 1990s. **METHODS:** We compiled data on life expectancy, socioeconomic status, and demographic characteristics for 211 county units in the 51 U.S. metropolitan areas with matching data on fine-particulate air pollution for the late 1970s and early 1980s and the late 1990s and early 2000s. Regression models were used to estimate the association between reductions in pollution and changes in life expectancy, with adjustment for changes in socioeconomic and demographic variables and in proxy indicators for the prevalence of cigarette smoking. **RESULTS:** A decrease of 10 microg per cubic meter in the concentration of fine particulate matter was associated with an estimated increase in mean (+/- SE) life expectancy of 0.61+/-0.20 year (P=0.004). The estimated effect of reduced exposure to pollution on life expectancy was not highly sensitive to adjustment for changes in socioeconomic, demographic, or proxy variables for the prevalence of smoking or to the restriction of observations to relatively large counties. Reductions in air pollution accounted for as much as 15% of the overall increase in life expectancy in the study areas. **CONCLUSIONS:** A reduction in exposure to ambient fine-particulate air pollution contributed to significant and measurable improvements in life expectancy in the United States.

**Kamdar, O., W. Le, et al. (2008). "Air pollution induces enhanced mitochondrial oxidative stress in cystic fibrosis airway epithelium." FEBS Lett 582(25-26): 3601-6.** We studied the effects of airborne particulate matters (PM) on cystic fibrosis (CF) epithelium. We noted that PM enhanced human CF bronchial epithelial apoptosis, activated caspase-9 and PARP-1; and reduced mitochondrial membrane potential. Mitochondrial inhibitors (4,4-diisothiocyantostilbene-2,2'-disulfonic acid, rotenone and thenoyltrifluoroacetone) blocked PM-induced generation of reactive oxygen species and apoptosis. PM upregulated pro-apoptotic Bad, Bax, p53 and p21; and enhanced mitochondrial localization of Bax. The anti-apoptotic Bcl-2, Bcl-xl, Mcl-1 and Xiap remained unchanged; however, overexpression of Bcl-xl blocked PM-induced apoptosis. Accordingly, we provide the evidence that PM enhances oxidative stress and mitochondrial signaling mediated apoptosis via the modulation of Bcl family proteins in CF.

**Nadadur, S. S., N. Haykal-Coates, et al. (2009). "Endothelial effects of emission source particles: acute toxic response gene expression profiles." Toxicol In Vitro 23(1): 67-77.** Air pollution epidemiology has established a strong association between exposure to ambient particulate matter (PM) and cardiovascular outcomes. Experimental studies in both humans and laboratory animals support varied biological mechanisms including endothelial dysfunction as potentially a central step to the elicitation of cardiovascular events. We therefore hypothesized that relevant early molecular alterations on endothelial cells should be assessable in vitro upon acute exposure to PM components previously shown to be involved in health outcomes. Using a model emission PM, residual oil fly ash and one of its predominant constituents (vanadium-V),

we focused on the development of gene expression profiles to fingerprint that particle and its constituents to explore potential biomarkers for PM-induced endothelial dysfunction. Here we present differential gene expression and transcription factor activation profiles in human vascular endothelial cells exposed to a non-cytotoxic dose of fly ash or V following semi-global gene expression profiling of approximately 8000 genes. Both fly ash and its prime constituent, V, induced alterations in genes involved in passive and active transport of solutes across the membrane; voltage-dependent ion pumps; induction of extracellular matrix proteins and adhesion molecules; and activation of numerous kinases involved in signal transduction pathways. These preliminary data suggest that cardiovascular effects associated with exposure to PM may be mediated by perturbations in endothelial cell permeability, membrane integrity; and ultimately endothelial dysfunction.

**Sun, Q., P. Yue, et al. (2008). "Air pollution exposure potentiates hypertension through reactive oxygen species-mediated activation of Rho/ROCK." Arterioscler Thromb Vasc Biol 28(10): 1760-6.** OBJECTIVE: Fine particulate matter <2.5 microm (PM(2.5)) has been implicated in vasoconstriction and potentiation of hypertension in humans. We investigated the effects of short-term exposure to PM(2.5) in the angiotensin II (AII) infusion model. METHODS AND RESULTS: Sprague-Dawley rats were exposed to PM(2.5) or filtered air (FA) for 10 weeks. At week 9, minipumps containing AII were implanted and the responses studied over a week. Mean concentration of PM(2.5) inside the chamber was 79.1±7.4 microg/m<sup>3</sup>. After AII infusion, mean arterial pressure was significantly higher in PM(2.5)-AII versus FA-AII group. Aortic vasoconstriction to phenylephrine was potentiated with exaggerated relaxation to the Rho-kinase (ROCK) inhibitor Y-27632 and increase in ROCK-1 mRNA levels in the PM(2.5)-AII group. Superoxide (O<sub>2</sub><sup>·-</sup>) production in aorta was increased in the PM(2.5)-AII compared to the FA group, inhibitable by apocynin and L-NAME with coordinate upregulation of NAD(P)H oxidase subunits p22(phox) and p47(phox) and depletion of tetrahydrobiopterin. In vitro exposure to ultrafine particles (UFP) and PM(2.5) was associated with an increase in ROCK activity, phosphorylation of myosin light chain, and myosin phosphatase target subunit (MYPT1). Pretreatment with the nonspecific antioxidant N-acetylcysteine and the Rho kinase inhibitors (Fasudil and Y-27632) prevented MLC and MYPT-1 phosphorylation by UFP suggesting a O<sub>2</sub><sup>·-</sup>-mediated mechanism for PM(2.5) and UFP effects. CONCLUSIONS: Short-term air pollution exaggerates hypertension through O<sub>2</sub><sup>·-</sup>-mediated upregulation of the Rho/ROCK pathway.

**Min, K. B., J. Y. Min, et al. (2008). "The relationship between air pollutants and heart-rate variability among community residents in Korea." Inhal Toxicol 20(4): 435-44.** Air pollution, both particulate and gaseous, is known to cause adverse health effects and is associated with increased cardiovascular mortality and morbidity. With a growing recognition in the importance of the autonomic nervous system in air pollution, we examined the effects of air pollutants, namely, particulate matter (PM<sub>10</sub>), sulfur dioxide (SO<sub>2</sub>), and nitric dioxide (NO<sub>2</sub>), on cardiac autonomic function by measuring heart-rate variability (HRV) among community residents. This study was conducted at Taean Island, located off the southern coast of South Korea; 1349 subjects (596 males and 753 females) were included in this analysis. Subjects

responded to the interview about general characteristics and an HRV examination was conducted. Exposure data were collected from the Environmental Management Corporation during the same period of HRV measurement. Linear regression analyses were carried out to evaluate the association over 72 h, and the parameters of HRV indices were presented as the percentage change. The exposures to PM(10), SO<sub>2</sub>, and NO<sub>2</sub> were associated with reduced HRV indices, and significant decreases in the standard deviation of the normal to normal interval (SDNN) and low frequency (LF) domain effect, and the effect was largely continued until 12 h. Our results suggest that air pollutants stimulate the autonomic nervous system and provoke an imbalance in cardiac autonomic control. Thus, these subclinical effects may lead to pathological consequences, particularly in high-risk patients and susceptible subjects.

**Stafoggia, M., J. Schwartz, et al. (2008). "Does temperature modify the association between air pollution and mortality? A multicity case-crossover analysis in Italy." Am J Epidemiol 167(12): 1476-85.** Adverse health effects of particulate matter <10 microm in aerodynamic diameter (PM(10)) and high temperatures are well known, but the extent of their interaction on mortality is less clear. This paper describes effect modification of temperature in the PM(10)-mortality association and tests the hypothesis that higher PM(10) effects in summer are due to enhanced exposure to particles. All deaths of residents of nine Italian cities between 1997 and 2004 were selected. The case-crossover approach was adopted to estimate the effect of PM(10) on mortality by season and temperature level. Three strata of temperature corresponding to low, medium, and high "ventilation" were identified, and the interaction between PM(10) and temperature within each stratum was examined. Season and temperature levels strongly modified the PM(10)-mortality association: for a 10-microg/m<sup>3</sup> variation in PM(10), a 2.54% increase in risk of death in summer (95% confidence interval: 1.31, 3.78) compared with 0.20% (95% confidence interval: -0.08, 0.49) in winter. Analysis of the interaction between PM(10) and temperature within temperature strata resulted in positive but, in most cases, nonstatistically significant coefficients. The authors found much higher PM(10) effects on mortality during warmer days. The hypothesis that such an effect is attributable to enhanced exposure to particles in summer could not be rejected.

**Tamagawa, E., N. Bai, et al. (2008). "Particulate matter exposure induces persistent lung inflammation and endothelial dysfunction." Am J Physiol Lung Cell Mol Physiol 295(1): L79-85.** Epidemiologic and animal studies have shown that exposure to particulate matter air pollution (PM) is a risk factor for the development of atherosclerosis. Whether PM-induced lung and systemic inflammation is involved in this process is not clear. We hypothesized that PM exposure causes lung and systemic inflammation, which in turn leads to vascular endothelial dysfunction, a key step in the initiation and progression of atherosclerosis. New Zealand White rabbits were exposed for 5 days (acute, total dose 8 mg) and 4 wk (chronic, total dose 16 mg) to either PM smaller than 10 μm (PM(10)) or saline intratracheally. Lung inflammation was quantified by morphometry; systemic inflammation was assessed by white blood cell and platelet counts and serum interleukin (IL)-6, nitric oxide, and endothelin levels. Endothelial dysfunction was assessed by vascular response to acetylcholine (ACh) and sodium nitroprusside (SNP). PM(10) exposure increased lung macrophages (P<0.02), macrophages containing particles

( $P < 0.001$ ), and activated macrophages ( $P < 0.006$ ). PM(10) increased serum IL-6 levels in the first 2 wk of exposure ( $P < 0.05$ ) but not in weeks 3 or 4. PM(10) exposure reduced ACh-related relaxation of the carotid artery with both acute and chronic exposure, with no effect on SNP-induced vasodilatation. Serum IL-6 levels correlated with macrophages containing particles ( $P = 0.043$ ) and ACh-induced vasodilatation ( $P = 0.014$  at week 1,  $P = 0.021$  at week 2). Exposure to PM(10) caused lung and systemic inflammation that were both associated with vascular endothelial dysfunction. This suggests that PM-induced lung and systemic inflammatory responses contribute to the adverse vascular events associated with exposure to air pollution.

**Yatera, K., J. Hsieh, et al. (2008). "Particulate matter air pollution exposure promotes recruitment of monocytes into atherosclerotic plaques." Am J Physiol Heart Circ Physiol 294(2): H944-53.** Epidemiologic studies have shown an association between exposure to ambient particulate air pollution  $< 10$  microm in diameter (PM(10)) and increased cardiovascular morbidity and mortality. We previously showed that PM(10) exposure causes progression of atherosclerosis in coronary arteries. We postulate that the recruitment of monocytes from the circulation into atherosclerotic lesions is a key step in this PM(10)-induced acceleration of atherosclerosis. The study objective was to quantify the recruitment of circulating monocytes into vessel walls and the progression of atherosclerotic plaques induced by exposure to PM(10). Female Watanabe heritable hyperlipidemic rabbits, which naturally develop systemic atherosclerosis, were exposed to PM(10) (EHC-93) or vehicle by intratracheal instillation twice a week for 4 wk. Monocytes, labeled with 5-bromo-2'-deoxyuridine (BrdU) in donors, were transfused to recipient rabbits as whole blood, and the recruitment of BrdU-labeled cells into vessel walls and plaques in recipients was measured by quantitative histological methodology. Exposure to PM(10) caused progression of atherosclerotic lesions in thoracic and abdominal aorta. It also decreased circulating monocyte counts, decreased circulating monocytes expressing high levels of CD31 (platelet endothelial cell adhesion molecule-1) and CD49d (very late antigen-4 alpha-chain), and increased expression of CD54 (ICAM-1) and CD106 (VCAM-1) in plaques. Exposure to PM(10) increased the number of BrdU-labeled monocytes adherent to endothelium over plaques and increased the migration of BrdU-labeled monocytes into plaques and smooth muscle underneath plaques. We conclude that exposure to ambient air pollution particles promotes the recruitment of circulating monocytes into atherosclerotic plaques and speculate that this is a critically important step in the PM(10)-induced progression of atherosclerosis.

**Totlandsdal, A. I., M. Refsnes, et al. (2008). "Particle-induced cytokine responses in cardiac cell cultures--the effect of particles versus soluble mediators released by particle-exposed lung cells." Toxicol Sci 106(1): 233-41.** Increased levels of particulate matter have been associated with adverse effects in the respiratory as well as the cardiovascular system. The biological mechanisms behind these associations are still unresolved. Among potential mechanisms, particulate matter-associated cardiac effects may be initiated by inhaled small-sized particles, particle components and/or mediators related to inflammation that translocate into the pulmonary circulation. In the present study cytokine responses (interleukin [IL]-6, IL-1beta, and tumor necrosis factor [TNF]-alpha) of primary rat cardiomyocytes and cardiofibroblasts in

mono- and cocultures induced by direct exposure to particles, were compared with cytokine responses induced by mediators released by particle-exposed primary rat epithelial lung cells (conditioned media). Cells were exposed to a model ultrafine particle (ultrafine carbon black, Printex 90) and in selected experiments to an urban air particle sample (SRM 1648, St Louis, MO). In lung cell cultures both particle types induced release of IL-6 and IL-1beta, whereas TNF-alpha was only detected upon exposure to St Louis particles. The release of IL-6 by cardiac cells was strongly enhanced upon exposure to conditioned media, and markedly exceeded the response to direct particle exposure. IL-1, but not TNF-alpha, seemed necessary, but not sufficient, for this enhanced IL-6 release. The role of IL-1 was demonstrated by use of an IL-1 receptor antagonist that partially reduced the effect of the conditioned media, and by a stimulating effect on the cardiac cell release of IL-6 by exogenous addition of IL-1alpha and IL-1beta. These in vitro findings lend support to the hypothesis that particle-induced cardiac inflammation and disease may involve lung-derived mediators.

**Totlandsdal, A. I., T. Skomedal, et al. (2008). "Pro-inflammatory potential of ultrafine particles in mono- and co-cultures of primary cardiac cells." Toxicology 247(1): 23-32.**

Inhalation of particulate air pollution has been associated with increased risks for cardiovascular mortality and morbidity, but the underlying mechanisms are still under discussion. One possible pathway may be that inhaled particles cross the air-blood barrier and interact directly with cardiac tissue. The aim of the present study was to examine the pro-inflammatory potential of particles in cardiac cells. Mono- and co-cultures of primary adult male Wistar (Han) rat cardiomyocytes (CMs) and cardiofibroblasts (CFs) were exposed to increasing concentrations of ultrafine (<100nm) carbon black particles (Printex 90). Expression and release of cytokines (IL-6, IL-1beta and TNF-alpha) were measured by using quantitative real-time PCR and ELISA, respectively. Cytotoxicity was estimated by measuring cellular release of lactate dehydrogenase (LDH). A particle concentration-dependent increase in IL-6 release was observed in both CM mono- and co-cultures (EC(50) approximately 57microg/ml). Furthermore, IL-6 levels detected in both control and particle-exposed co-cultures were synergistically increased compared to mono-cultures (10-19-fold, dependent on the exposure). Experiments with contact and non-contact co-cultures indicate that direct cellular contact is of key importance for the enhanced release of IL-6 in co-cultures. An apparent particle-induced release of IL-1beta was only detected in co-cultures. The release of TNF-alpha was low and did not seem notably influenced by particle exposure. Treatment with an IL-1 receptor antagonist apparently eliminated the particle-induced release of IL-6. In conclusion, ultrafine particles have a pro-inflammatory potential in primary cardiac cells. Furthermore, IL-1 seems critical in triggering particle-induced release of IL-6. These pro-inflammatory responses may be elicited when particles are translocated into the pulmonary circulation upon inhalation or administered intravascularly during medical procedures.

**Lee, S. J., S. Hajat, et al. (2008). "A time-series analysis of any short-term effects of meteorological and air pollution factors on preterm births in London, UK." Environ Res 106(2): 185-94.** Although much is known about the incidence and burden of preterm birth, its biological mechanisms are not well understood. While several studies have suggested that high

levels of air pollution or exposure to particular climatic factors may be associated with an increased risk of preterm birth, other studies do not support such an association. To determine whether exposure to various environmental factors place a large London-based population at higher risk for preterm birth, we analyzed 482,568 births that occurred between 1988 and 2000 from the St. Mary's Maternity Information System database. Using an ecological study design, any short-term associations between preterm birth and various environmental factors were investigated using time-series regression techniques. Environmental exposures included air pollution (ambient ozone and PM(10)) and climatic factors (temperature, rainfall, sunshine, relative humidity, barometric pressure, and largest drop in barometric pressure). In addition to exposure on the day of birth, cumulative exposure up to 1 week before birth was investigated. The risk of preterm birth did not increase with exposure to the levels of ambient air pollution or meteorological factors experienced by this population. Cumulative exposure from 0 to 6 days before birth also did not show any significant effect on the risk of preterm birth. This large study, covering 13 years, suggests that there is no association between preterm births and recent exposure to ambient air pollution or recent changes in the weather.

**Rankin, J., T. Chadwick, et al. (2009). "Maternal exposure to ambient air pollutants and risk of congenital anomalies." Environ Res 109(2): 181-7.**

Studies have suggested an association between maternal exposure to ambient air pollution and risk of congenital anomaly. The aim of this study is to investigate the association between exposure to black smoke (BS; particulate matter with aerodynamic diameter <4 microm(3)) and sulphur dioxide (SO(2)) during the first trimester of pregnancy and risk of congenital anomalies. We used a case-control study design among deliveries to mothers resident in the UK Northern health region during 1985-1990. Case data were ascertained from the population-based Northern Congenital Abnormality Survey and control data from national data on all births. Data on BS and SO(2) from ambient air monitoring stations were used to average the total pollutant exposure during the first trimester of pregnancy over the daily readings from all monitors within 10 km of the mother's residence. Logistic regression models estimated the association via odds ratios. A significant but weak positive association was found between nervous system anomalies and BS (OR=1.10 per increase of 1000 microm(3) total BS; 95% CI: 1.03, 1.18), but not with other anomaly subtypes. For SO(2), a significant negative association was found with congenital heart disease combined and patent ductus arteriosus: OR significantly <1 for all quartiles relative to the first quartile. The relationship between SO(2) levels and other anomaly subtypes was less clear cut: there were either no significant associations or a suggestion of a U-shaped relationship (OR significantly <1 for moderate compared to lowest levels, but not with high SO(2) levels). Overall, maternal exposure to BS and SO(2) in the Northern region had limited impact on congenital anomaly risk. Studies with detailed exposure assessment are needed to further investigate this relationship.

**Son, J. Y., Y. S. Cho, et al. (2008). "Effects of air pollution on postneonatal infant mortality among firstborn infants in Seoul, Korea: case-crossover and time-series analyses." Arch Environ Occup Health 63(3): 108-13.** Infants are known to be susceptible to the adverse health effects of ambient air pollution. The authors examined the relationship between air pollution and

postneonatal mortality from all causes among firstborn infants in Seoul, Korea, during 1999-2003, using both case-crossover and time-series analyses. Using a bidirectional control-sampling approach, the authors compared the effects of various types of air pollution on postneonatal mortality. The relative risk of postneonatal mortality from all causes was 1.000 (95% confidence interval [CI] = 0.998-1.002) for particulate matter with a diameter <10 µm, 1.002 (95% CI = 0.994-1.009) for nitrogen dioxide, 1.015 (95% CI = 0.973-1.058) for sulfur dioxide, 1.029 (95% CI = 0.833-1.271) for carbon monoxide, and 0.984 (95% CI = 0.977-0.992) for ozone for each 1-unit increase of air pollution level in the 1:6 control selection scheme. The authors observed a positive association between air pollution and infant daily mortality except for the studied particulate matter and ozone, although it was not statistically significant. They obtained similar results in the time-series analysis. The risk of postneonatal infant death from all causes was positively associated with all studied air pollutants except ozone. The authors also confirmed that the bidirectional method with many controls will give a more efficient estimator than will a method with fewer controls.

**Epton, M. J., R. D. Dawson, et al. (2008). "The effect of ambient air pollution on respiratory health of school children: a panel study." *Environ Health* 7: 16.** Adverse respiratory effects of particulate air pollution have been identified by epidemiological studies. We aimed to examine the health effects of ambient particulate air pollution from wood burning on school-age students in Christchurch, New Zealand, and to explore the utility of urine and exhaled breath condensate biomarkers of exposure in this population. **METHODS:** A panel study of 93 male students (26 with asthma) living in the boarding house of a metropolitan school was undertaken in the winter of 2004. Indoor and outdoor pollution data was continuously monitored. Longitudinal assessment of lung function (FEV1 and peak flow) and symptoms were undertaken, with event studies of high pollution on biomarkers of exposure (urinary 1-hydroxypyrene) and effect (exhaled breath condensate (EBC) pH and hydrogen peroxide concentration). **RESULTS:** Peak levels of air pollution were associated with small but statistically significant effects on lung function in the asthmatic students, but not healthy students. No significant effect of pollution could be seen either on airway inflammation and oxidative stress either in healthy students or students with asthma. Minor increases in respiratory symptoms were associated with high pollution exposure. Urinary 1-hydroxypyrene levels were raised in association with pollution events by comparison with low pollution control days. **CONCLUSION:** There is no significant effect of ambient wood-smoke particulate air pollution on lung function of healthy school-aged students, but a small effect on respiratory symptoms. Asthmatic students show small effects of peak pollution levels on lung function. Urinary 1-hydroxypyrene shows potential as a biomarker of exposure to wood smoke in this population; however measurement of EBC pH and hydrogen peroxide appears not to be useful for assessment of population health effects of air pollution. Some of the data presented in this paper has previously been published in Kingham and co-workers *Atmospheric Environment*, 2006 Jan; 40: 338-347 (details of pollution exposure), and Cavanagh and co-workers *Sci Total Environ*. 2007 Mar 1;374(1):51-9 (urine hydroxypyrene data).

**Ma, L., M. Shima, et al. (2008). "Effects of airborne particulate matter on respiratory**

**morbidity in asthmatic children." J Epidemiol 18(3): 97-110.** The effects of airborne particulate matter (PM) are a major human health concern. In this panel study, we evaluated the acute effects of exposure to PM on peak expiratory flow (PEF) and wheezing in children. METHODS: Daily PEF and wheezing were examined in 19 asthmatic children who were hospitalized in a suburban city in Japan for approximately 5 months. The concentrations of PM less than 2.5  $\mu\text{m}$  in diameter (PM(2.5)) were monitored at a monitoring station proximal to the hospital. Moreover, PM(2.5) concentrations inside and outside the hospital were measured using the dust monitor with a laser diode (PM(2.5(LD))). The changes in PEF and wheezing associated with PM concentration were analyzed. RESULTS: The changes in PEF in the morning and evening were significantly associated with increases in the average concentration of indoor PM(2.5(LD)) 24 h prior to measurement (-2.86 L/min [95%CI: -4.12, -1.61] and -3.59 L/min [95%CI: -4.99, -2.20] respectively, for 10- $\mu\text{g}/\text{m}^3$  increases). The change in PEF was also significantly associated with outdoor PM(2.5(LD)) concentrations, but the changes were smaller than those observed for indoor PM(2.5(LD)). Changes in PEF and concentration of stationary-site PM(2.5) were not associated. The prevalence of wheezing in the morning and evening were also significantly associated with indoor PM(2.5(LD)) concentrations (odds ratios = 1.014 [95%CI: 1.006, 1.023] and 1.025 [95%CI: 1.013, 1.038] respectively, for 10- $\mu\text{g}/\text{m}^3$  increases). Wheezing in the evening was significantly associated with outdoor PM(2.5(LD)) concentration. The effects of indoor and outdoor PM(2.5(LD)) remained significant even after adjusting for ambient nitrogen dioxide concentrations. CONCLUSION: Indoor and outdoor PM(2.5(LD)) concentrations were associated with PEF and wheezing among asthmatic children. Indoor PM(2.5(LD)) had a more marked effect than outdoor PM(2.5(LD)) or stationary-site PM(2.5).

**O'Connor, G. T., L. Neas, et al. (2008). "Acute respiratory health effects of air pollution on children with asthma in US inner cities." J Allergy Clin Immunol 121(5): 1133-1139 e1.** Children with asthma in inner-city communities may be particularly vulnerable to adverse effects of air pollution because of their airways disease and exposure to relatively high levels of motor vehicle emissions. OBJECTIVE: To investigate the association between fluctuations in outdoor air pollution and asthma morbidity among inner-city children with asthma. METHODS: We analyzed data from 861 children with persistent asthma in 7 US urban communities who performed 2-week periods of twice-daily pulmonary function testing every 6 months for 2 years. Asthma symptom data were collected every 2 months. Daily pollution measurements were obtained from the Aerometric Information Retrieval System. The relationship of lung function and symptoms to fluctuations in pollutant concentrations was examined by using mixed models. RESULTS: Almost all pollutant concentrations measured were below the National Ambient Air Quality Standards. In single-pollutant models, higher 5-day average concentrations of NO<sub>2</sub>, sulfur dioxide, and particles smaller than 2.5  $\mu\text{m}$  were associated with significantly lower pulmonary function. Higher pollutant levels were independently associated with reduced lung function in a 3-pollutant model. Higher concentrations of NO<sub>2</sub> and particles smaller than 2.5  $\mu\text{m}$  were associated with asthma-related missed school days, and higher NO<sub>2</sub> concentrations were associated with asthma symptoms. CONCLUSION: Among inner-city children with asthma, short-term increases in air pollutant concentrations below the National Ambient Air

Quality Standards were associated with adverse respiratory health effects. The associations with NO<sub>2</sub> suggest that motor vehicle emissions may be causing excess morbidity in this population.

**Odajima, H., S. Yamazaki, et al. (2008). "Decline in peak expiratory flow according to hourly short-term concentration of particulate matter in asthmatic children." Inhal Toxicol 20(14): 1263-72.** The aim was to investigate the effects of the 3-h mean concentration of suspended particulate matter (SPM) on peak expiratory flow (PEF) in asthmatic children. Subjects were 4- to 11-year-old boys and girls with asthma in Fukuoka, Japan. Daily measurements of PEF were made between April 2002 and March 2003. PEF was measured morning and evening. To assess the association between 3-h mean concentrations of SPM and morning PEF and evening PEF separately, we used generalized estimating equations. All models took into consideration seasonal effects: modified effects were examined using a two-level indicator variable for the warmer months (April through September) and the colder months (October through March). Among the 70 asthmatic children, 44 were boys. In warmer months, declines in morning PEF for 10 microg/m<sup>3</sup> differences in 3-h concentration of SPM measured at 2 a.m. to 5 a.m. of the same day and 11 p.m. to 2 a.m. and 8 p.m. to 11 p.m. of the previous day were -0.78 L/min (95% CI: -1.40, -0.16), -0.61 L/min (-1.18, -0.05) and -0.73 L/min (-1.32, -0.15), respectively. Results were robust even after adjustment for other air pollutants. We also found that declines in evening PEF were weakly associated with increases in 3-h concentrations of SPM in warmer months, but the associations were not statistically significant. In colder months we did not find any robust association between SPM and morning/evening PEF. In conclusion, an increased 3-h concentration of SPM is associated with declines in PEF in warmer months.

**Tecer, L. H., O. Alagha, et al. (2008). "Particulate matter (PM(2.5), PM(10-2.5), and PM(10)) and children's hospital admissions for asthma and respiratory diseases: a bidirectional case-crossover study." J Toxicol Environ Health A 71(8): 512-20.** Epidemiological studies reported adverse effects of air pollution on the prevalence of respiratory diseases in children. The purpose of this study was to examine the association between air pollution and admissions for asthma and other respiratory diseases among children who were younger than 15 yr of age. The study used data on respiratory hospital admissions and air pollutant concentrations, including thoracic particulate matter (PM(10)), fine (PM(2.5)), and coarse (PM(10-2.5)) particulate matter in Zonguldak, Turkey. A bidirectional case-crossover design was used to calculate odds ratios for the admissions adjusted for daily meteorological parameters. Significant increases were observed for hospital admissions in children for asthma, allergic rhinitis (AR), and upper (UPRD) and lower (LWRD) respiratory diseases. All fraction of PM in children showed significant positive associations with asthma admissions. The highest association noted was 18% rise in asthma admissions correlated with a 10-microg/m<sup>3</sup> increase in PM(10-2.5) on the same day of admissions. The adjusted odds ratios for exposure to PM(2.5) with an increment of 10 microg/m<sup>3</sup> were 1.15 and 1.21 for asthma and allergic rhinitis with asthma, respectively. PM(10) exerted significant effects on hospital admissions for all outcomes, including asthma, AR, UPRD, and LWRD. Our study suggested a greater effect of fine and coarse PM on asthma hospital admissions compared with PM(10) in children.

**Van Roosbroeck, S., R. Li, et al. (2008). "Traffic-related outdoor air pollution and respiratory symptoms in children: the impact of adjustment for exposure measurement error." Epidemiology 19(3): 409-16.** Outdoor concentrations of soot and nitrogen dioxide (NO<sub>2</sub>) outside of schools have been associated with children's respiratory and eye symptoms. We assessed how adjustments for measurement error affect these associations. **METHODS:** Concentrations of air pollutants outside children's schools were validated by personal measurements of exposure to traffic-related air pollution. We estimated prevalence ratios of 4 health outcomes (current wheeze, conjunctivitis, phlegm, and elevated total serum immunoglobulin E) using school outdoor measurements, and then adjusted for measurement error using the personal exposure data and applying a regression calibration method. The analysis adjusting for measurement error was carried out using a main study/external validation design. **RESULTS:** Adjusting for measurement error produced effect estimates related to soot and NO<sub>2</sub> that were 2 to 3 times higher than in the original study. The adjusted prevalence ratio for current phlegm was 5.3 (95% confidence interval = 1.2-23) for a 9.3 microg/m<sup>3</sup> increase in soot, and 3.8 (1.0-14), for a 17.6 microg/m<sup>3</sup> increase in NO<sub>2</sub>, compared with the original results of 2.2 (1.3-3.9) and 1.8 (1.1-2.8), respectively. Corrections were of similar magnitude for the prevalence of current wheeze, current conjunctivitis, and total elevated total immunoglobulin E. **CONCLUSIONS:** The estimated effects of outdoor air pollution on respiratory and other health effects in children may be substantially attenuated when based on exposure measurements outside schools instead of personal exposure.

**Ballester, F., S. Medina, et al. (2008). "Reducing ambient levels of fine particulates could substantially improve health: a mortality impact assessment for 26 European cities." J Epidemiol Community Health 62(2): 98-105.** Recently new European policies on ambient air quality--namely, the adoption of new standards for fine particulate matter (PM(2.5)), have generated a broad debate about choosing the air quality standards that can best protect public health. The Aphis network estimated the number of potential premature deaths from all causes that could be prevented by reducing PM(2.5) annual levels to 25 microg/m<sup>3</sup>, 20 microg/m<sup>3</sup>, 15 microg/m<sup>3</sup> and 10 microg/m<sup>3</sup> in 26 European cities. The various PM(2.5) concentrations were chosen as different reductions based on the limit values proposed by the new European Directive, the European Parliament, the US Environmental Protection Agency and the World Health Organization, respectively. The Aphis network provided the health and exposure data used in this study. The concentration-response function (CRF) was derived from the paper by Pope et al (2002). If no direct PM(2.5) measurements were available, then the PM(10) measurements were converted to PM(2.5) using a local or an assumed European conversion factor. We performed a sensitivity analysis using assumptions for two key factors--namely, CRF and the conversion factor for PM(2.5). Specifically, using the "at least" approach, in the 26 Aphis cities with more than 40 million inhabitants, reducing annual mean levels of PM(2.5) to 15 microg/m<sup>3</sup> could lead to a reduction in the total burden of mortality among people aged 30 years and over that would be four times greater than the reduction in mortality that could be achieved by reducing PM(2.5) levels to 25 microg/m<sup>3</sup> (1.6% vs 0.4% reduction) and two times greater than a reduction to 20 microg/m<sup>3</sup>. The percentage reduction could grow by more than

seven times if PM(2.5) levels were reduced to 10 microg/m<sup>3</sup> (3.0% vs 0.4%). This study shows that more stringent standards need to be adopted in Europe to protect public health, as proposed by the scientific community and the World Health Organization.

**Lee, S. J., S. Hajat, et al. (2008). "A time-series analysis of any short-term effects of meteorological and air pollution factors on preterm births in London, UK." Environ Res 106(2): 185-94.** In this case 482,568 births were analyzed in a London based study. The births occurred between 1988 and 2000 and data was obtained from the St. Mary's Maternity Information System database. Short-term associations between preterm birth and various environmental factors were assessed with time-series regression techniques. Environmental exposures included air pollution (ambient ozone and PM10) and climatic factors (temperature, rainfall, sunshine, relative humidity, barometric pressure, and largest drop in barometric pressure). In addition to exposure on the day of birth, cumulative exposure up to 1 week before birth was investigated. The risk of preterm birth did not increase with exposure to the levels of ambient air pollution or meteorological factors experienced by this population. Cumulative exposure from 0 to 6 days before birth also did not show any significant effect on the risk of preterm birth. This large study, covering 13 years, suggests that there is no association between preterm births and recent exposure to ambient air pollution or recent changes in the weather.

**Rankin, J., T. Chadwick, et al. (2009). "Maternal exposure to ambient air pollutants and risk of congenital anomalies." Environ Res 109(2): 181-7.** Studies have suggested an association between maternal exposure to ambient air pollution and risk of congenital anomaly. The aim of this study is to investigate the association between exposure to black smoke (BS; particulate matter with aerodynamic diameter <4 microg/m<sup>3</sup>) and sulphur dioxide (SO<sub>2</sub>) during the first trimester of pregnancy and risk of congenital anomalies. We used a case-control study design among deliveries to mothers resident in the UK Northern health region during 1985-1990. Case data were ascertained from the population-based Northern Congenital Abnormality Survey and control data from national data on all births. Data on BS and SO<sub>2</sub> from ambient air monitoring stations were used to average the total pollutant exposure during the first trimester of pregnancy over the daily readings from all monitors within 10 km of the mother's residence. Logistic regression models estimated the association via odds ratios. A significant but weak positive association was found between nervous system anomalies and BS (OR=1.10 per increase of 1000 microg/m<sup>3</sup> total BS; 95% CI: 1.03, 1.18), but not with other anomaly subtypes. For SO<sub>2</sub>, a significant negative association was found with congenital heart disease combined and patent ductus arteriosus: OR significantly <1 for all quartiles relative to the first quartile. The relationship between SO<sub>2</sub> levels and other anomaly subtypes was less clear cut: there were either no significant associations or a suggestion of a U-shaped relationship (OR significantly <1 for moderate compared to lowest levels, but not with high SO<sub>2</sub> levels). Overall, maternal exposure to BS and SO<sub>2</sub> in the Northern region had limited impact on congenital anomaly risk. Studies with detailed exposure assessment are needed to further investigate this relationship.

**Son, J. Y., Y. S. Cho, et al. (2008). "Effects of air pollution on post-neonatal infant**

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

**mortality among firstborn infants in Seoul, Korea: case-crossover and time-series analyses." Arch Environ Occup Health 63(3): 108-13.)** The relationship between air pollution and post-neonatal mortality from all causes among firstborn infants in Seoul, Korea, during 1999-2003 was studied. Both case-crossover and time-series analyses with a bidirectional control-sampling approach were used to compare the effects of air pollutants on post-neonatal mortality. The relative risk of post-neonatal mortality from all causes was 1.000 (95% confidence interval [CI] = 0.998-1.002) for PM10, 1.002 (95% CI = 0.994-1.009) for NO2, 1.015 (95% CI = 0.973-1.058) for SO2, 1.029 (95% CI = 0.833-1.271) for CO, and 0.984 (95% CI = 0.977-0.992) for O3 for each 1-unit increase of air pollution level in the 1:6 control selection scheme. The authors observed a positive association between air pollution and infant daily mortality except for the studied particulate matter and ozone, although it was not statistically significant. They obtained similar results in the time-series analysis. The risk of post-neonatal infant death from all causes was positively associated with all studied air pollutants except ozone. Therefore, while a positive association was observed between PM10 and post-neonatal mortality the findings were not statistically significant.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

## Comments from Dr. Ellis Cowling

**Individual Comments on the December 2008**  
**First External Review Draft of the**  
**Integrated Science Assessment (ISA) for Particulate Matter**  
  
**and the February 2009 document titled:**  
**Particulate Matter National Ambient Air Quality Standards:**  
**Scope and Methods Plan for Urban Visibility Impact Assessment**

Dr. Ellis Cowling

**My specific assignment for review of the ISA for PM was Chapter 9 – Ecosystem and Welfare Effects.**

The set of 10 Charge Questions provided in John Vandenberg’s letter of January 30, 2009 to Holly Stallworth included the following questions with regard to Chapter 9:

How useful and complete is the scientific evidence presented in Chapter 9 regarding the effects of Atmospheric PM on the environment, including (a) effects on visibility, (b) effects on individual organisms, (c) direct and indirect effects on ecosystems, (d) effects on materials, and (e) effects on climate? To what extent do the discussions and integration of evidence correctly represent and clearly communicate the state of the science?

### **General Comments on the Presentation of Scientific Evidence Regarding Effects of PM on Visibility, Individual Organisms, Ecosystems, Materials, and Climate in the ISA**

It is excellent that each of the “**Summary and Conclusion**” statements on pages 9-1, 9-5, 9-6, and 9-7 begins with a simple declarative sentence written in **bold type** indicating that “**The evidence is sufficient to infer a causal relationship between ambient PM and**” [all five significant welfare effects of ambient PM covered in Chapter 9] **visibility, individual organisms, ecosystems, materials, and climate**. These statements set the stage for a through-going discussion about the body of scientific evidence that supports these very firm statements of causality. That is very good!

Also useful (but frequently lacking in precision of communication because of poor definitions of terms and the absence of a list of acronyms for the whole ISA) are the series of detailed presentations of scientific evidence regarding the effects of PM on all five of these same significant welfare effects including:

- **visibility** on pages 9-7 through 9-86;  
mechanisms of atmospheric deposition on pages 9-86 through 9-106 especially with regard to effects of airborne PM on

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

- **individual organisms** on pages 9-106 through 9-119,
- **ecosystems** on pages 9-119 through 9-127,
- **materials** on pages 9-127 through 9-132;  
and finally effects of PM on various aspects of
- **climate** on pages 9-132 through 9-156.

Fortunately, some of these detailed presentations fall more closely within the areas of special competence of some of my fellow PM CASAC Panel Members who also were assigned to review Chapter 9. For example, Bill Malm, regarding PM effects on **visibility**, and also David Grantz, Rich Poirot, and Lowell Ashbaugh regarding PM effects on **materials** and **climate**. Thus, I am looking forward to listening very attentively to their Individual Comments on some of these special topics in contrast to the discussion about both **mechanisms of atmospheric deposition** and effects of PM constituents on **individual organisms** and **ecosystems** that are more close to my own areas of special competence.

#### **Detailed Comments on Some Limitations in the Clarity and Completeness of Chapter 9.**

**First with regard to Clarity:** Most of my difficulty in assessing the quality of the information provided in Chapter 9 is a result of a significant lack of precision in the terminology and lack of definitions of the acronyms used in this chapter.

On pages 9-1 through 9-7 for example, it is not clear what is meant by the acronym EC or the terms “crustal material,” “urban excess,” “urban excess carbonaceous PM,” Midwest nitrate bulge,” “four light extinction components,” “hydrated sulfate particles,” etc.

Clear definitions of terms and especially the acronyms used in any ISA document are essential to understanding the science that is being assessed. Many more definitions of terms and a complete list of all acronyms used in all parts should be included in the Second External Review Draft of this document.

Much confusion in many different parts of Chapter 9 (and in the other chapters of this ISA) are caused by sloppiness in the use (and many different meanings) of the word “level”). The word “level” is sometimes used to mean “air concentration,” other times to mean “amount,” other times to mean “consistency,” other times to mean “altitude” (distance above sea level),” other times to mean “unchanged,” other times to mean “degrees” or “extent” or “types” of visibility impairment, species of organisms, or concepts of physiology or ecology, and still other times to mean “tolerance” or “acceptability” (for example in attitudes of citizens about haziness in the atmosphere). My advice is to use any or all of these other terms when they avoid the ambiguity that so often accompanies use of the word “level.”

An illustration of a biological concept that also is presented very inadequately is found in the following paragraph near the bottom of page 9-5 within the **Summary of Effects on Individual Organisms and Ecosystems** in the **Summary and Conclusions** section of Chapter 9:

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

“Many of the most important effects [of PM] occur in the soil. The soil environment is one of the most dynamic sites of biological diversity in nature. It is inhabited by microbial communities of bacteria, fungi, and actinomycetes. These organisms are essential participants in the nutrient cycles that make nutrients available for plant uptake. Changes in the soil environment that influence the role of bacteria and fungi in nutrient cycling determine plant and ultimately ecosystem response.”

These five sentences (and especially the last sentence in this paragraph) give readers the unintended impression that scientific studies of “microbial communities” in soil have been shown to be affected by airborne PM [and, by implication, that the many and diverse “non-microbial” organisms in soil -- such as rodents, insects, earth worms, nematodes, viruses, and roots of higher plants themselves – all have been studied but have NOT been shown to be affected by airborne PM].

Surprisingly, these very same ideas are presented very much more adequately in the detailed discussions on pages 9-106 through 9-119 regarding **Effects on Individual Organisms** and on pages 9-119 through 9-127 regarding **Effects on Ecosystems**.

**Second with regard to Completeness:** During the recent efforts to streamline the NAAQS review processes, the following general policy question was recommended as a guide during the NAAQS review processes:

*What scientific evidence and/or scientific insights have been developed since the last review to indicate if the current public-health based and/or the current public-welfare based NAAQS need to be revised or if alternative levels, indicators, statistical forms, or averaging times of these standards are needed to protect public health with an adequate margin of safety and to protect public welfare?”*

Since the Clean Air Act defines “public welfare” to include the effects of air pollution on “visibility, ... and personal comfort and wellbeing.” and the present draft ISA for particulate matter concludes that “**The evidence is sufficient to infer a causal relationship between ambient PM and visibility impairment,**” the most directly relevant policy questions to be resolved by the current NAAQS-review process for PM are:

- 1) “**Does the current public-welfare based NAAQS need to be revised?**” and, if so
- 2) “**What alternative levels, indicators, statistical forms, or averaging times of the secondary standard for PM should be considered in order to protect public welfare?**”

The only parts of the present First External Review Draft of the ISA for PM that deal directly with the current secondary standard for PM are:

- 1) The very confusing paragraph on lines 8 through 16 on page 1-9 of Chapter 1, and
- 2) The section of Chapter 9 titled “**Urban Visibility Valuation and Preference**” on pages 9-74 through 9-83 where a preliminary attempt is made to:

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

“separate out the aesthetic and wellbeing components associated with the visibility condition produced by a given level of air pollution when assessing the need for additional regulation to protect [against] the public welfare effect[s] of visibility under the Secondary NAAQS.” This was attempted in the present ISA by analyzing results from the Urban Visibility Preference Studies completed in recent years in Denver, Colorado, Phoenix, Arizona, British Columbia, Canada, and Washington, DC (see pages 9-76 through 9-81 in the ISA).

Thus, I recommend that the Second External Review Draft of the ISA for PM and the First Draft Risk and Exposure Assessment for PM include sections that deal explicitly with the two questions printed in italic type in the above paragraph.

-----

**My specific assignment for review of the February 2009 document titled: “*Particulate Matter National Ambient Air Quality Standards: Scope and Methods Plan for Urban Visibility Impact Assessment*” was Chapter 3 – Quantitative Visual Air Quality Assessment.**

Having carefully reviewed all three chapters in this document, I was generally satisfied with the approach outlined in this Scope and Methods Plan but recommend that earnest consideration also be given to including sections in the Second External Review Draft of the ISA for PM to be completed in July 2009 and the First Review Draft of the Urban Visibility Impact Assessment (UVA) to be completed in September 2009 that deal explicitly with the following two specific policy questions:

- 1) “***Does the current public-welfare based NAAQS need to be revised?***” and, if so
- 2) “***What alternative levels, indicators, statistical forms, and averaging times of the secondary standard for PM should be considered in order to protect public welfare?***”

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

## **Comments from Dr. James Crapo**

### PMISA Comments

The EPA Staff are to be congratulated on producing a comprehensive and well designed overview of issues related to ambient particulate matter including the substantial amount of research on PM published since the last CASAC review of this topic. In general, the integrative tables and figures are clear and presented in a form that allows consideration of the scope of the data with respect to potential adverse health effects for PM.

#### *Chapter 2 – Integrative Health Effects*

This chapter provides an integrative summary and assesses the likelihood of causal relationships for specific health effects with respect to PM exposure. I like the general approach the EPA has used, including their five-level hierarchy for causal determination. This is a rigorous approach to the central issue that has been requested on multiple previous ISA documents. The EPA staff has critically reviewed the relevant literature on this topic and has made concrete recommendations regarding their conclusions with regard to causality. I applaud the approach of starting with a list of the key health effects and a firm statement with regard to conclusions of causality and following this by a brief description of the key findings supporting the conclusions. Hopefully, this will become a model for future ISA documents.

In general, I agree with the causality conclusions with regard to the key health effects and I agree with the selection of the health effects for emphasis in this chapter. The focus of this chapter is on short- and long-term exposures to PM<sub>10</sub> and PM<sub>2.5</sub>. This implies that a firm decision has been made not to consider regulatory recommendations with regard to PM<sub>10-2.5</sub>. I believe we will ultimately need to evaluate epidemiologic and animal studies data with regard to PM<sub>10-2.5</sub> in order to understand the contributory effects of coarse particulates. Data on PM<sub>10-2.5</sub> is incorporated in other chapters on Health Effects but not brought forward to the summary and conclusions in Chapter 2. From a regulatory perspective today this may be appropriate; however, I would recommend that at least a summary section on PM<sub>10-2.5</sub> be included in Chapter 2.

I also liked section 2.2.3 on constituents or sources linked to health outcomes. There are insufficient data to derive concrete conclusions; however, there are suggestions that specific constituents or sources will eventually be linked with specific health effects. This is likely to be an area that will expand in future reviews of PM.

#### *Chapter 5 – Possible Pathways/Modes of Action*

This chapter provides a reasonable review of the possible pathways or modes of action of particulates in contributing to adverse health effects. The chapter is short, focused and provides a number of alternative frameworks to consider the mechanisms of actions of particulates. I found this chapter useful. Part of its strength is its brevity and its liberal use of illustrations. I would recommend keeping this approach for this section of the ISA.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

*Chapter 7 – Integrated Health Effects of Long-Term PM Exposure*

Chapter 7 is thorough and well written. It provides an excellent overview of the long-term health effects of PM exposure. An important strength of this chapter is the creation of Figures that clearly illustrate the combined primary findings with each of the topics (i.e., cardiovascular and systemic risks, respiratory risks, reproductive and developmental risks, cancer risks and overall mortality. This is well done in Figure 7.8. Figure 7.1 is also a very useful summary figure. I would recommend that summary figures be created for each of the sections – even where the data suggests no significant effect. The written summaries in each section are appropriate; however, I think there should be tables or figures that summarize and compare the primary data for each section.

Chapter 7 would be strengthened by shortening it, achieving greater focus on the new findings, and a focus on the summary tables as suggested above.

### **Comments from Dr. Douglas Crawford-Brown**

#### **Review of the Document: Particulate Matter National Ambient Air Quality Standards: Scope and Methods Plan for Health Risk and Exposure Assessment**

Douglas Crawford-Brown  
03-20-09

I was not assigned to a specific charge question, so I chose those that I felt are most in line with my area of expertise. A general comment is that the document is longer than I might have hoped to see. The other ISAs (for other NAAQS) produced recently have set a trend of significantly reducing the amount of material that would have been covered under the older Criteria Document system. This PM ISA reverses that trend. I realize there is a LOT of PM material available in the literature, but I still would have liked to see a little more distillation of the literature down to the key studies and points before production of the ISA.

1. The framework for causal determination and judging the overall weight of evidence is presented in Chapter 1. Is this framework appropriately applied for this PM ISA? How might the application of the framework be improved for PM effects?

There is now emerging a consistent framework being applied across the various ISAs, so it is becoming easier to see the reasoning behind the causal conclusions drawn in this and other ISAs. There are quibbles I might have with the particular framework chosen, but it is as good as any other I have seen and at least serves to draw the analyst's attention to the key questions to be addressed. It appropriately separates a judgment of causality from one of there being a C-R function. The categories of strength of causality are sufficient and clearly defined, so I found it easy to understand why the analyst chose to place a given study and effect into a given category. Overall, I am satisfied with this system as a sufficient tool, and recommend no further tweaking, which allows everyone to now settle on examining the particular conclusions being drawn within the framework.

The only point that continues to concern me is that the judgments of causality still tend to be categorical: PM is or is not causally connected to effect X. I think a better system is one in which the degree of support for such a claim changes as the level of exposure changes. It would be useful to see how the support changes as one approaches low levels being considered for regulatory targets. There is some hint of this throughout the application of the framework, but it is never made explicit, especially in Chapter 1.

2. Chapter 2 presents the integrative summary and conclusions from the health effects evidence at the beginning of the ISA with the evidence characterized in detail in subsequent chapters. (Environmental and public welfare effects evidence is evaluated and summarized in

Chapter 9.) Is this a useful and effective summary presentation? How does the Panel view the inclusion in Chapter 2 of only health categories with causal determinations of (a) likely to be a causal relationship or (b) a causal relationship?

I found Chapter 2 very useful, and it went a long way towards alleviating the general concern I mentioned above in regards to the length of the document. I feel it is appropriate to summarize only the findings from the studies that fall into these two causal categories, although mention can be made of studies/effects that did not meet these criteria (without providing summaries of these). I found the discussion of the implications of exposure and dosimetry for the conduct and interpretation of epidemiologic studies useful, which was a real strength of this ISA, especially since this is one pollutant for which a lot can be said on these points.

The discussion in the chapter concerning composition of particles was adequate but not especially insightful. The summary table was good, but I would have expected a bit more of an assessment of, and justification for, a decision to either consider or not consider composition in any final risk assessments that might be conducted based on the ISA. I must admit that I read the REA first, and so was primed for this issue in turning to the ISA (the wrong order in which to read these), but still I expected more in the ISA on this point.

The chapter correctly summarizes the susceptibility and vulnerability issues raised in subsequent chapters, and so serve this issue well. I was less happy with the discussion of C-R curves, feeling it needed more of a mathematical treatment in this chapter. I always expect a discussion of such curves – whether in summary or in the complete chapter being summarized – to include data plotted to visually indicate where there is a clear positive slope and where this disappears into then noise of studies, and some indication of the shape of the curve at all levels of exposure. Chapter 2 does not go very far down this road and so is less effective as a summary than I would have wanted.

4. The dosimetry of PM is discussed in Chapter 4. The primary focus is on factors that might lead to differences in deposition and clearance between individuals, species, and as a function of the physicochemical properties of particles. Is the review of basic dosimetric principles presented in sufficient detail? Are the new particle translocation data adequately and accurately described? Recognizing an overall goal of producing a clear and concise chapter, are there topics that should added or receive additional discussion? Similarly, are there topics that should be shortened or removed? To what extent does the Panel find Annex B appropriate, adequate and effective in supporting the ISA?

I was comfortable with Chapter 4. It provided an overview of mechanisms of deposition and clearance at just enough detail to give the reader an understanding of the issues. It was perhaps left to the reader to see the implications for study interpretation, or for the drawing of conclusions on causal connections in particular studies, but the information is there to help in this

regard. I found the level of technical detail also appropriate for a topic that can quickly become too mathematical for many readers.

The one area in which I would suggest a bit of improvement is in the inhomogeneity of deposition and clearance, especially in regards to carinal ridges. This is mentioned by never really explored.

I kept returning to Annex B for detail, and so I suppose this indicates the Annex served its purpose. I found it contain a lot of useful information, even if it was a bit difficult to sort through it to find exactly the point being raised in the chapter itself.

8. What are the views of the Panel on the definitions of susceptibility and vulnerability in Chapter 8? Are the characteristics included within the broad susceptibility and vulnerability categories appropriate and consistent with the definitions used?

I am comfortable with these definitions. This is a topic that always gets a lively debate, and people tend to have some pretty entrenched positions on the issue (with good arguments to support their positions). But in the end, what matters is that the terms are well defined both verbally and operationally, and then applied consistently. I feel the authors have satisfied these criteria in the ISA and so the characteristics considered serve the intended purpose as well as any other set of definitions might.

10. This first external review draft PM ISA is of substantial length and reflects the copious amount of research recently conducted on PM. EPA has attempted to succinctly present and integrate the policy-relevant scientific evidence for the review of the PM NAAQS. Does the Panel have opinions on how the document can be shortened without eliminating important and necessary content?

This is back to my original comment. The document was too long for me to read in its entirety. I instead read about 500 pages of it in enough detail to determine whether the information was sufficient. This leaves me with the uncomfortable position of worrying about whether the other 500 or so pages might contain information or analyses that would influence the interpretations and judgments I had formed in the sections I did read in detail.

Chapter 3 strikes me as a chapter that could usefully be pruned by half. It reads a bit like a data dump, with every bit of information to hand put into the document just in case someone might find it of interest. In most of the cases of page after page of data, I had little sense that these data were telling a story that would be needed later in conducting an exposure assessment or interpreting epidemiologic studies. This doesn't mean the data will not prove useful at some point – only that the authors didn't focus my attention onto specific reasons WHY the data might be important.

By way of contrast, there is about the same amount of data available in the literature on particle deposition and clearance, but Chapter 4 is a third the size of Chapter 3. Chapter 4 also does a better job of focusing the reader's attention onto the significance of the data being presented.

I saw little in Chapter 5 that could be deleted without loss of significant content, and so would not expect cuts to be made here.

Chapter 6 is the longest by far. I found myself focusing almost entirely on summary tables and figures, rather than the exhaustive page-after-page listings of characteristics of specific studies. The chapter could easily be shortened by half without loss of any content that the reader will care about. As it is written currently, it suffers from all of the problems of the older criteria documents. This shortening would be accomplished by provision of even better summary tables and figures, perhaps with a Comments column to explain any special features of a study the author wants to highlight.

In fact, Chapter 6 is even longer than the 200+ pages contained within it, because much of Chapter 7 is a similar presentation of study results. The purpose of Chapter 7 is to provide an integrative approach, but I could find little of that in the chapter. It became instead yet another place to serve as a repository of exhaustive study descriptions. There should be little need to describe studies by this chapter, and certainly no need to present even more data. The chapter should instead focus on how the materials of earlier chapters, including the dosimetry considerations, can be integrated into a consistent picture of which effects are causal, and at what levels of exposure, and under what conditions. There are places where Chapter 7 starts to approach this goal, but then the reader is plunged back again into listings of studies. This chapter is the one most in need of not shortening per se, but a better focus on the purpose of the chapter.

## **Comments from Dr. David Grantz**

REGARDING December 2008 draft of

### **USEPA Integrated Science Assessment for Particulate Matter** **(First External Review Draft)**

The document as a whole makes a real contribution and is well done, quite readable, and relatively complete. The following represent comments or suggestions for revision of the ISA, not in priority order.

1. It would be helpful to provide a list of acronyms. Further, it would be useful to describe briefly air monitoring programs such as AQS (page 2-2, line 11) to present the characteristics that make them particularly suitable for the specific analysis under discussion.
2. The approach of Chapter 9, which deals with all welfare effects considered together, differs considerably from that of Chapter 2 (and subsequent supporting chapters 3-8), which deals with discrete health endpoints. There seems to have been little effort to apply the criteria of causality laid out earlier (e.g. Table 1-2), even for visibility which is the strongest welfare component in terms of available data. Indeed visibility is a nearly discrete endpoint which could be separated into its own chapter. There is a sense that other components of welfare effects have been determined prior to preparation of this ISA to be non-“policy relevant”, and therefore have received little critical attention.

Inconsistencies between the treatment of health and welfare effects are numerous. It is interesting that (page 9-113, line 23-26) the most interesting plants are said to be the tolerant members of the population, whereas in the health sections (and in the legislation) it is the most sensitive and most vulnerable members of the population that are to receive greatest attention. A committed search for the most sensitive receptors for specific endpoints (such as the sentinel species considered on page 9-116) might help to better focus the discussion of welfare effects and aid the search for quantifiable C-R relationships that might guide development of a separately determined secondary standard for PM.

A detailed chart of causality begins each subsection in Section 2.3, and would be useful if added for each subsection of Chapter 9. The three non-visibility findings of “inferred causality”--between PM and effects on organisms and ecosystems, on materials, and on climate are much too general, analogous to a finding of causality between PM and human health, rather than the various endpoints laid out in Chapters 2-8. Further, it is unclear whether the phrase (Section 9.2.2) of “sufficient to infer a causal relationship” has exactly the same meaning as the phrase “sufficient evidence to conclude that a causal relationship exists” that appears in Chapter 2. This should be clarified.

A consequence of this general approach to welfare effects is that data that would have been considered to contribute to a finding of “likely causal” or “contributing to biological plausibility” in the health context, receive little more than an uncritical listing in the welfare context. For example (page 9-108, line 1-12), the analysis of PM by Sheesley et al. (2004) might be used to infer likely causality or biological plausibility, but is instead summarized as “does not provide the data needed to assess risk”. Similarly, data such as that presented by Oliveira and Pampulha (2006; page 9-118, line 28-30) and other studies might be amenable to semi-quantitative analysis, yielding estimates of soil concentrations, inferred rates of deposition, and potentially even atmospheric concentrations of PM. The challenges laid out for ecosystem data (page 9-120, line 26 through page 9-121, line 2) are not so different from the early stages of health effects investigations. These and other possible opportunities could be pursued throughout the welfare section, as a means to begin development of the C-R relationships required to support a secondary PM standard. A more critical reading of the available literature for quantitative relationships may lead closer to C-R relationships than seems possible from the current presentation. The discussion in Section 9.2.2, for example, states generalities but never discusses the direction or magnitude of PM-induced changes. The text does not effectively support the finding of causality that begins the section.

3. The material in Chapter 9 could be reorganized to emphasize discrete endpoints, and possible causal relationships related to each. Visibility could be placed in its own, better focused chapter. Material presented in the current chapter 9 on characterization of particles could be relocated to precede the health sections, and the material on deposition to extensive landscapes could be placed earlier where it might inform discussion of resuspension and personal PM clouds in the health context. This would isolate the material on effects on organisms and effects on ecosystems or communities, which could be considered together or separately, but in the context of discrete endpoints. This would focus the discussion and remove the need for abrupt transitions, such as that into discussion of deposition in Section 9.4 (page 9-83).

The material on toxic metals should be assembled as needed for causality determinations within each endpoint. In the current draft, discussion of the nature and role of heavy metals is diffused throughout the chapter, but never brought to a focus or conclusion. As above, this would avoid the abrupt introduction of metals in Table 9-3 (page 9-89) and in the text at top of page 9-90, where it appears out of place.

The discussion of organic pollutants is somewhat weak. These materials represent direct threats to organisms and ecosystems, and substantial indirect threats to food chains including human food supply. As such they may become central to the determination of a secondary PM standard. This discussion (page 9-114, line 27 to 9-116, line 10) is really a discussion of semivolatile compounds. These have unique transport properties, characterized by repeated distillation on surfaces as a function of diel trends in

temperature. This is not well captured by the text. The discussion of fugacity, which is defined at a constant temperature (page 9-116, line 5-7), does not capture the well known leap-frog behavior of SVOCs across the surface of the earth. The discussion of POPs (page 9-103, line 30-31), is confusing with regards to the air plant response route (really a contact route), and uptake by above ground plant tissue, (also a contact route) in contrast to the distinction between the two (top of page 9-104).

The discussion of bioaccumulation of organics (page 9-124 to 9-125) can be made quite a bit more quantitative, even if causality cannot be demonstrated at this stage.

4. There is some uncertainty about mercury residence times, and about the oxidation state of Hg (page 9-101-102, lines 31-6) under discussion at each point. It would be useful to state explicitly what combining forms Hg(II) is found in, and (e.g. page 9-103, top) whether gas or particle, and what oxidation state, is under discussion at each point.
5. The use of visibility as a surrogate for welfare effects may have unintended consequences. This is considered more fully in comments regarding the visibility plan. In order to keep regulatory environments similar for day and night hours, a movement toward modeled or virtual visibility is to be encouraged. This avoids the application of dark viewing techniques (e.g. page 9-12, line 11), and allows explicit use of developed relationships between visibility and parameters such as RH, to be applied at all hours. In the limit, this could avoid use of dark periods to dump particulates that exceed the secondary standard.

Visibility as a standard metric is confounded by regionally differing policy relevant backgrounds, and regionally differing popular perceptions of acceptable visibility. In the ISA this is shown for residents of Chilliwack and Abbotsford (Page 9-80). Buy-in of regulated communities may be compromised by regionally differing standards for PM mass, to achieve differing standards of visibility.

6. The treatment of urban visibility valuation (Section 9.3.5 is written rather loosely, and never reaches a focus or conclusion. The acronym, VAQ, is used in several incompatible senses. The definition (page 9-74, line 24) improbably equates impairment with quality. VAQ is considered something to be seen (page 9-75, line 12), and then more appropriately as a quality that can be better or worse. The modifier, “low”, could be inserted prior to “VAQ” (line 25-26), since it is not likely that high VAQ would diminish a sense of well being.
7. The discussion of dry deposition (particularly page 9-86, lines 20-26 and page 9-90, lines 17-28) is somewhat vague and incomplete. The roles of sedimentation and resuspension are not considered adequately. The discussion is not entirely consistent with Figure 9-52. The consideration of eddy covariance techniques (page 9-88, line 34) might reconsider whether coarse particles are transported efficiently in high frequency eddies.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

8. Page 9-47, line 8, in wintertime it may be that oxidizing potential to convert NO<sub>x</sub> to nitric acid is limiting. While this appears to be the implication of this sentence, this is an important point that requires further elaboration with respect to mechanisms and consequences for air quality.
9. The discussion regarding exchange of PM-borne materials across vegetated surfaces (page 9-95, line 1-3) is quite important and generally well done here. The concept of measured dry deposition exceeding bulk deposition requires further elaboration, particularly as to measurement technique for the two parameters. In the discussion of exchange of mercury (page 9-97, line 26-27) the two forms of deposition that are mentioned are both dry deposition, in contrast to the text.
10. The discussion of individual species near the Harjavalta smelter (page 9-126, line 21-24) is of interest, but should be placed in the context of the section heading—Ecosystem Function. The isolated consideration of a few insect and spider species, without reference to their roles in the ecosystem, is analogous to a statement that influenza is good for buzzards. Misses the point a bit.
11. The discussion of direct impacts of coarse particles (page 9-108 to 9-109) is incomplete. Many consequences are mediated by disruption of leaf cuticle and waxes, from pathogen defense to control of water loss. Surface pH is important, particularly for colonization, but also for wax degradation. These need to be elaborated upon. It is not clear, and at least requires better referencing, that salt is generally taken up through abrasions in the shoot rather than through the roots, and that this leads to plants leaning away from the ocean.
12. Minor comments:
  - Page 9-2, line 5, there appears a discontinuity between discussion of pristine skies and polluted ones.
  - Page 9-5, line 13, it is not correctly parallel to refer to PM deposition as a pollutant (PM is the pollutant).
  - Page 9-6, line 2, N should be Ni.
  - Page 9-7, line 11, BC is introduced here for possibly the first time. Is this the same as EC, introduced earlier? Either way there needs to be a definition given.
  - Figure 9-3 (page 9-14), it is unclear what 1.5 stands for in the internal labels for each line.
  - Figure 9-31 (page 9-49) it is unclear what the three sizes of pie charts in the legends, and the numbers 20, 60, and 100 represent.
  - Page 9-22, line 10-14, better to provide a mathematical equation. The form and intent of this verbally described transformation is unclear.
  - Page 9-48, line 8, should be “east” end of gorge.
  - Figures 9-38 to 9-43 (Pages 9-58 to 9-64) are quite difficult to interpret. The legend and caption can both be made more user friendly.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

Page 9-105, line 14, it is unclear whether petrogenic refers to petroleum or geology.

Page 9-113, line 12-22, a better distinction should be made between tire dust and road dust.

Page 9-127, line 27-28, use of a bioluminescence assay is a type of bioassay that directly measures the toxicity of the mixture of metals under consideration. This should be presented in the context of such direct effect measurements.

Page 9-136, line 24, the ratio of diffuse to total solar radiation is lowest at noon.

Page 9-139, line 4-5, it is not clear what factor of 2 refers to.

Page 9-140, line 26-28, the reduction in radiative forcing over the 80 year recover period requires further explanation here.

## Comments from Dr. Joseph Helble

### Comments on Chapter 3, ISA CASAC Review, Integrated Science Assessment for Particulate Matter April 2009

1. Particle morphology may affect particle transport properties, depending upon particle size. It will also affect particle surface area regardless of size. Because surface area and particle transport properties may both affect exposure, discussion of current understanding of morphology or surface area distributions would be beneficial. This is acknowledged in the ISA in section 3.2 (line 23, page 3-3) where shape along with size and composition is listed as a variable characteristic of atmospheric PM.
2. This point is reinforced in Section 3.4.13. page 3-24, where it is noted that “methods are being developed to measure the surface area of ultrafine particles (line 23).” No additional discussion of surface area is provided. It arises again on p. 3-37 line 9, where “particle shape” is listed as one possible cause of differences noted among samples at supersites.
3. A listing of acronyms and abbreviations is needed at the start of the ISA. Some are not defined at all, others are not defined until they have been used many times in earlier sections. A listing is included in the Scope and Methods documents and is also warranted in the ISA.
4. Fly ash from combustion of coal, oil, and wood can also produce particles in the PM1.0 size range and is therefore also a potential source of Fine particles (Table 3-1, page 3-6). It is in part a source of the metals that are listed in the table.
5. Similarly, primary PM (“minerals”) can be emitted as fly ash from fossil fuel and wood combustion, a source category listed in Table 3-1 but not in Table 3-2. The tables are largely consistent, but review for full agreement would be helpful.
6. A brief narrative description of the sources contributing to the “miscellaneous” categories of PM 10 and PM 2.5 sources (Figure 3-2) should be included.
7. Section 3.3.2.2 page 3-12 line 18 the sentence beginning Robinson et al. (2007a) needs clarification. Presumably the statement indicates that direct measurements of combustion source emissions do not accurately capture all of the semi-volatile organic content, leading to an underestimation of the contribution of combustion sources to semi-volatile organics observed in PM.
8. P. 3-37 line 20 discussed an artifact when QBT filtering was used. Earlier in this section, page 3-21, only QBQ and TBQ are mentioned as commonly used methods. If QBT is not a typo, it should also be discussed on p. 3-21 when the other filter methods are described.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

9. Comments on the higher maxima noted in Table 3-11 PM 10 distributions from AQ data would be helpful.
10. Page 3-104 notes that “compositional profiles used in receptor models can be extensive.” And variable? Worth addressing explicitly if the literature suggests differences would affect conclusions drawn from CMB models.
11. Page 3-146 line 2 the sentence beginning “Particle chemistry” is confusing. It implies that chemical composition affects particle deposition behavior. While there is certainly a link between composition and size it is not a determinative relationship, and clearly it is size (and structure) that primarily affect deposition patterns.
12. The discussion relating exposure assessment and socioeconomic status makes points regarding neighborhood scale monitor distribution that do not appear to be consistent with the data in the subsequent tables. Specifically, lines 20-23 page 3-161 argue that “neighborhood scale SES issues are not shown to be well represented.” The inference drawn from the text as written is that monitors are not sufficiently well distributed, at the neighborhood level, in neighborhoods of lower SES status. A comparison of data in Tables 3-30 through 3-32 indicates, however, that a higher percentage of the less-educated population lives within 1 km of a monitor than is true for other educational attainment levels. It may be reasonable to argue that a higher concentration of monitors is needed in these neighborhoods, but the data as presented do not appear to suggest disparity in their siting.
13. Typographical Errors
  - a. Page 3-8 line 9 the word “exhaust” should be inserted after “vehicle”
  - b. Page 3-27 line 23 “from” should be inserted between “Except” and “some”
  - c. Page 3-66 the figures present correlation as fractional values, the text describes them in percentage terms. The discussion should be made consistent with the figures.
  - d. Page 3-72 Figure 3-30 caption indicates “Pittsburgh,” but the legend indicates “Philadelphia. This needs to be corrected.
  - e. Page 3-85 line 10 insert “are” between “than” and “ultrafine”
  - f. Page 3-103 line 24 insert appropriate table numbers
  - g. Page 3-114 line 12 delete “described”
  - h. Page 3-115 line 112 sentence beginning “In this section” unclear – comma needed after “average” - ?
  - i. Page 3-115 line 28 “have” should be changed to “has”
  - j. Page 3-116 line 5 a colon needed after “components”
  - k. Figures 3-61 through 3-63 need to be made larger and sharper
  - l. Page 3-141 line 14 space needed between “be” and “evaluated”
  - m. Page 3-143 line 28 “suggests” should be “suggest”

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

- n. Page 3-145 line 2 “utilities” should be “utility”
- o. Page 3-148 Line 9 the “88” in concentrations needs to be deleted
- p. Page 3-149 line 1 Figure 3-71 should be changed to Figure 3-74
- q. Page 3-150 line 10 insert “and” before “indoor”
- r. Page 3-152 line 2 insert ) after the first Zn

## **Comments from Dr. Rogene Henderson**

Comments on PM ISA, December, 2008

### Chapter 1--Framework

I thought the explanation of the EPA framework for causal determination was well done. It will provide the basis for future NAAQS documents for all criteria pollutants. In the future this standard approach might be placed in an appendix, but it is appropriate to include it in the PM ISA text for discussion.

### Chapter 2--Integrative Health Effects Overview

I found this to be a useful chapter. I thought the chapter needed a few more words about the health effects of short and long term exposures to ultrafine PM and PM<sub>10-2.5</sub> particles, not just the one sentence at the bottom of page 2-11 saying we have inadequate evidence to infer causal relationships. The chapter might also be expanded to include the summary sections from Chapters 6 and 7 (see suggestion below) and serve as the health effects section of the ISA, with large parts of chapters 6 and 7 as appendices. That is not to say that Chapters 6 and 7 are not important. Those chapters contain the detailed information upon which Chapter 2 is based. But if one valued a shorter ISA, one could use an expanded Chapter 2 with appendices for the health effects. For my own benefit, I made a table that included each of the four particle sizes for rows and each of the major endpoints as columns, with the resultant cells showing the finding in terms of causality. I did this for both the short term and the long-term exposures. Such a simple summary table would be appropriate in Chapter 2.

### Chapters 6 and 7:

These are highly valuable summaries of the health effects of short and long term exposures to PM conducted since the last review. I found the sections labeled "Overall Summary and Causal Determination" found at the end of each health effects section especially useful. I wonder if you might combine these sections with what is in Chapter 2, edit it to remove redundancies, put the details of the new studies described in Chapters 6 and 7 in Appendices, and use the expanded Chapter 2 as the Health Effects chapter.

## Comments from Dr. Phil Hopke

### PM ISA Comments

This Chapter is generally well written. However, there are a number of small additions and corrections that would improve its overall content and presentation.

Xia and Hopke (2006) observed seasonal variation for the two major diastereoisomers coming from isoprene oxidation with the concentrations occurring during the summer and the lowest concentrations occurring during the winter. The variation of the carbon contribution of 2-methyltetrols to OC was found to follow the same pattern as the concentration variation of 2-methyltetrols. During summer, the period of high photochemical activity, the maximum carbon contribution of 2-methyltetrols to OC was 2.8%.

It should be noted that the byproducts of terpene oxidation forming SOA are inherently oxidative in nature. Docherty et al. (2005) found that 47% to 85% of SOA mass is composed of peroxide compounds. Organic peroxides represent an important class of reactive oxygen species (ROS) that have high oxidizing potential and could cause oxidative stress in cells on which such particles deposit.

A major question is whether to persist in using a filter based method as the Federal Reference Method where we know that the current FRM for PM<sub>2.5</sub> has good precision, totally undefined accuracy and when operating perfectly provides data with 66% of the days unmeasured. I suggest that such a measurement protocol is no longer acceptable. It is critical to have essentially complete data capture, higher time resolved data, and measurements that better reflect the actual concentration of particulate matter that exists in the atmosphere without the unknown and unknowable losses of semivolatile materials that come from a 24 “equilibration” period. The document is currently silent on these fundamental flaws of the FRM approach while putting in detail on studies of how people try and replicate the inaccurate measurements known to be provided by the FRM. It is time for a change in paradigm and move to continuous monitors that can remove some of the particle-bound water without as drastically disturbing the other semivolatile components.

There should be some description of the Wagner and Leith passive monitors for PM<sub>10</sub> and PM<sub>10-2.5</sub>. Since the short-term standard for PM<sub>10</sub> has been eliminated, it would be possible to provide long term monitoring for PM<sub>10</sub> or PM<sub>10-2.5</sub> for many more locations using passive samplers and thus, they are worth discussing.

I find Figures 3-4 and 3-5 very hard to follow. They are described in a single sentence on page 3-29 and the point being made is left quite vague. Either clarify why the figures are there or remove them.

There is no discussion of trends in composition. We have data now from 2000 to 2008 at a number of locations across the US. Is the composition changing relative to the overall mass concentration?

There is no mention of the ultrafine measurements in Rochester (Jeong et al., 2004, 2006) looking at the seasonal variability in the diurnal patterns of ultrafines and distinguishing between vehicular, plume, and regional nucleation events.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

Although not widely used, Unmix should also be mentioned on Page 3-105. It is mentioned on 3-107, but the methods should be introduced together. Also it should be noted that PMF and Unmix have been applied to particle size distributions to obtain source identification of ultrafine particles.

An issue that is not presented is whether intercontinental dust events are really contributors to the PRB or just constitute unusual events. For example, there was a large Saharan dust storm in early July 2002 that contributed  $25 \mu\text{g}/\text{m}^3$  on July 1 and  $24 \mu\text{g}/\text{m}^3$  on July 2, 2002 (Lee et al., JGR 2006). It is logical to assign these well defined specific events to the PRB?

There have been useful new approaches to using satellite data to estimate fine particle exposure that are worth noting.

Estimating fine particulate matter component concentrations and size distributions using satellite-retrieved fractional aerosol optical depth: Part 1 - Method development

Liu Y, Koutrakis P, Kahn R: JOURNAL OF THE AIR & WASTE MANAGEMENT ASSOCIATION Volume: 57 Issue: 11 Pages: 1351-1359 Published: NOV 2007

Estimating fine particulate matter component concentrations and size distributions using satellite-retrieved fractional aerosol optical depth: Part 2 - A case study, Liu Y, Koutrakis P, Kahn R, et al. JOURNAL OF THE AIR & WASTE MANAGEMENT ASSOCIATION Volume: 57 Issue: 11 Pages: 1360-1369 Published: NOV 2007

It should be noted that one of the effects of ambient ozone when it infiltrates into indoor air is that it can produce new particle formation by reaction with the terpenes released by a variety of cleaning and personal care products. Weschler has published extensively on this subject.

#### Comments on Chapter 4

There has been some useful recent work on the penetration of fibrous particles (high aspect ratio) through head and TB airways.

##### **Record 1 of 6**

Wang, Z; Hopke, PK; Ahmadi, G; Cheng, YS; Baron, PA. 2008. Fibrous particle deposition in human nasal passage: The influence of particle length, flow rate, and geometry of nasal airway. *JOURNAL OF AEROSOL SCIENCE* 39 (12): 1040-1054..

**Author Full Name(s):** Wang, Zuocheng; Hopke, Philip K.; Ahmadi, Goodarz; Cheng, Yung-Sung; Baron, Paul A.

**DOI:** 10.1016/j.jaerosci.2008.07.008

---

##### **Record 2 of 6**

Zhou, Y; Su, WC; Cheng, YS. 2008. Fiber Deposition in the Tracheobronchial Region: Deposition Equations. *INHALATION TOXICOLOGY* 20 (13): 1191-1198..

**Author Full Name(s):** Zhou, Yue; Su, Wei-Chung; Cheng, Yung Sung

**DOI:** 10.1080/08958370802233082

---

##### **Record 3 of 6**

Zhou, Y; Su, WC; Cheng, YS. 2007. Fiber deposition in the tracheobronchial region: Experimental measurements. *INHALATION TOXICOLOGY* 19 (13): 1071-1078..

**Author Full Name(s):** Zhou, Yue; Su, Wei-Chung; Cheng, Yung Sung

**DOI:** 10.1080/08958370701626634

---

##### **Record 4 of 6**

Su, WC; Cheng, YS. 2006. Deposition of fiber in a human airway replica. *JOURNAL OF AEROSOL SCIENCE* 37 (11): 1429-1441..

**Author Full Name(s):** Su, Wei-Chung; Cheng, Yung Sung

**DOI:** 10.1016/j.jaerosci.2006.01.015

---

##### **Record 5 of 6**

Su, WC; Cheng, YS. 2006. Fiber deposition pattern in two human respiratory tract replicas. *INHALATION TOXICOLOGY* 18 (10): 749-760..

**Author Full Name(s):** Su, Wei-Chung; Cheng, Yung Sung

**DOI:** 10.1080/08958370600748513

---

##### **Record 6 of 6**

Su, WC; Cheng, YS. 2005. Deposition of fiber in the human nasal airway. *AEROSOL SCIENCE AND TECHNOLOGY* 39 (9): 888-901..

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

**DOI:** 10.1080/02786820500295685

## **Comments from Dr. Mort Lippmann**

### **Lippmann's Review Comments on Draft PM ISA – March 2009**

#### **Overall Comments:**

The draft PM ISA provides a reasonably thorough and balanced presentation of a voluminous and complex literature on ambient air PM and its health and environmental effects. The summations and judgments made therein are, for the most part, reasonable and well focused on the needs of the Agency for its mandated task of periodic reconsideration of the suite of PM NAAQS.

The most serious failing is the decision to organize the discussion as though PM<sub>10</sub> was a separate pollutant from PM<sub>2.5</sub> and PM<sub>10-2.5</sub>. It should be obvious that PM<sub>10</sub> is a mongrel mixture of the other two, and was only retained because of the limited database for the exposures to, and effects of, PM<sub>10-2.5</sub> and the need to retain some control of the PM<sub>10-2.5</sub> concentrations in the name of public health protection. At this point, the only reasonable way to remedy this problem in the next draft is to describe what is known about the makeup of PM<sub>10</sub> in the exposure atmosphere in any description of an association of measured PM<sub>10</sub> with a health-related effect. In some eastern US cities, where PM<sub>2.5</sub> is 90% of PM<sub>10</sub>, there will be little reason to implicate coarse particles in any association. By contrast, in some western US cities, where coarse PM accounts for 50% or more of PM<sub>10</sub>, effects associated with PM<sub>10</sub> are more likely to be due to coarse PM. The reader can then decide whether the effect associated with PM<sub>10</sub> is likely due to the fine or coarse components.

Other unfortunate decisions in the organization of the toxicology presentations were to include: 1) descriptions of the effects produced by exposures to diluted engine exhausts and other lab-generated mixtures in with the discussions of the effects of ambient air PM; and 2) descriptions of the effects produced by IT exposures to high doses with those of inhalation exposures at more realistic exposures. These more artificial exposures should be described, but in separate sections, with some discussion of what useful information they can provide.

My comments specific to each chapter of the draft ISA follow.

#### **Chapter 1:**

Overall: Very well done.

#### **Specific Comments:**

- p. 1-14, line 23      change “collected” to “retained”.
- p. 1-25, line 13      what is “edpolicy”?

#### **Chapter 2:**

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

Overall: Needs clarification and specific corrections.

Specific Comments:

p. 2-5, lines 13,22 what is “diel”?

p. 2-11, line 21,22 Change to “(i.e., cardiovascular morbidity and mortality, respiratory morbidity and mortality)”. It is exceedingly strange to omit cardiovascular mortality, especially for chronic exposure, where it is the biggest health impact of them all!

pp. 2-12 – 2-14: Section 2.3.1. As noted above in my first Overall Comment, it is very unfortunate and confusing to talk about effects of PM<sub>10</sub> without at least discussing what is known about the size distribution of the particular PM<sub>10</sub> mixture in each case. It would also be helpful to include any information on PM composition whenever it is known.

P. 2-20, lines 1-9 This brief summary of long-term exposure and excess mortality should be expanded to note that almost all of the excess is cardiovascular (Pope et al. 2004).

P. 2-22, Table 2-1. The Oil Combustion section should include the epidemiological studies cited in Lippmann et al. (2006) and Hedley et al. (2002).

### **Chapter 3:**

Overall: Provides a good summary review of important background material.

Specific Comment:

p. 3-8, line 9 insert “emissions” after “vehicle”.

### **Chapter 4:**

Overall: Provides a good summary review of important background material.

Specific Comments:

p. 4-5, line 15 change “particulates” to “particles”.

p. 4-7, line

p. 4-27, line 26 change “filter” to “filtered”.

p. 4-36, line 15 fix reference citation.

### **Chapter 5:**

Overall: Provides a good summary review of important background material.

Specific Comments: None

### **Chapter 6:**

Overall Comment: Provides a reasonably good summary review of important material, but needs some cleanup for careless errors.

Specific Comments:

- p. 6-3, line 13 change “affect” to “effect”.
- p. 6-3, line 31 change “is” to “are”.
- p. 6-4, line 23 change “linear” to “log-linear”.
- p. 6-5, line 2 change “the” to “an enriched”.
- p. 6-5, line 23 change “cyclone” to “centrifuge”.
- p. 6-5, line 29 insert “and modified by” before “Maciejczyk”.
- p. 6-6, line 16 insert “particles” after “exhaust”.
- p. 6-6, line 24 change “particulates” to “particles”.
- p. 6-6, line 25 insert influence of the” before “co-pollutants”.
- p. 6-19, line 7 change “Tuxedo, NY” to “Manhattan”.
- p. 6-21, line 11 This discussion of short-term changes in HR and HRV needs to be expanded to include the short-term changes reported by Chen and Hwang et al. (2005),
- p. 6-197, line 30 the paper by Sama et al. (Sama, P., Long, T.C., Hester, S., Tajuba, J., Parker, J., Chen, L-C., Veronesi, B. (2007). The cellular and genomic response of an immortalized microglia cell line (BV2) to concentrated ambient particulate matter. *Inhal. Toxicol.* 19:1079-1087).
- p. 6-247, Table 6-16 the Lippmann et al. reference at the beginning should be “2006”, not “2000”.

**Chapter 7:**

Overall: Provides a less than adequate summary review of important material. Did the authors run out of time to get it right?

Specific Comments:

- p. 7-1, Heading for Section 7.2 change to “**Cardiovascular and Systemic Morbidity Effects**”
- p. 7-2, line 24 define “CAC”.
- p. 7-3, line 9 define “CIMT”.
- p. 7-3, line 21 define “ABI”.
- p. 7-3, line 30 define “AAC”.
- p. 7-4, lines 3-14 Why start off this discussion with a paper that shows essentially no response?
- p. 7-5, lines 23-29 Why give such prominence to an IT study?
- p. 7-6, line 1 the Sun et al. (2005) paper cited at the start of this section, and the Sun et al. (2008) paper are important reports on aspects of NYU’s second 6-month subchronic inhalation exposure study. The results of the first such study were summarized by Lippmann et al. (2005a), and referred to, in part, as ‘an other project’ on lines 24 and 25

- of this page. The first study should be cited first, and reference to the Sun et al. (2005) paper should follow.
- p. 7-7, lines 23-24 “despite 85% of the total particle number concentration for PM<sub>2.5</sub> being comprised of ultrafine PM” is a truly nonsense statement. What were the authors trying to say here?
  - p. 7-7, line 30 How can anybody take seriously a study in which the “control” exposure to PM<sub>10</sub> was 50% of that in the “exposed”?
  - p. 7-8, lines 7-20 How can anybody take seriously a study in which such a high IT dose was administered?
  - p. 7-9, line 23 The Sun et al. (2008) and Reed et al. (2004; 2006; 2008) papers were **not** from the “same group”. The Sun et al. paper was based on a study performed at NYU, while the Reed et al. papers described work done at Lovelace (LRRI).
  - p. 7-9, line 24 “HWS” was not defined. [hard wood smoke?]
  - p. 7-10, line 9 “TAT” was not defined.
  - p. 7-12, lines 4-8 I am mystified that the effect for the preceding 60 days of exposure were reported rather than those for the preceding 30 days of exposure. The most interesting finding was that the effect increased with time up to 30 days, and then decreased!
  - p. 7-17, lines 14,15 Isn't a -45% decrease a 45% increase? Please clarify!
  - p. 7-17, line 21 Isn't this saying that PM<sub>10</sub> exposure was protective? Please clarify!
  - p. 7-23, line 6-8 The citation to Peters et al. (1999) is no longer informative, and should be deleted. This cross-sectional preliminary analysis does not, in any way, contradict the subsequent prospective cohort analyses of the same population by Gauderman et al. (2000, 2002, 2004).
  - p. 7-24, lines 1-3 The Avol et al. (2001) paper is not adequately presented. Not only were the kids moving to cleaner PM areas having greater lung development, but the kids moving to dirtier PM areas were having reduced lung development.
  - p. 7-39, line 15 The Gunnison and Chen (2005) paper was **not** a preliminary study, but was based on the exact same exposures cited in line 11.
  - p. 7-39, line 17-19 The Maciejczyk et al. (2005) study is a simultaneous (parallel) study of *in vitro* exposures on the same days as the subchronic inhalation exposures, but is not a “second” parallel study.
  - p. 7-104, Fig.7-8 Why weren't the Pope et al. (2002) lung cancer data depicted here?
  - p. 7-117, lines 4,5 Delete “likely to be”. The authors should have the courage to accept the overwhelming epidemiological evidence of excess annual mortality associated with annual average PM<sub>2.5</sub>, which is amply supported by the results of a series of subchronic PM<sub>2.5</sub> exposure studies in animals showing progressive changes in atherosclerotic plaque development and progressive deterioration of cardiac function.
  - p. 7-117, line 11 Change “short-term” to “short- and long-term”.

## Chapter 8

Overview: Provides a less than adequate summary review of extremely important material. Did the authors run out of time to get it right?

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

### Specific Comments

- p. 8-2, lines 23-26 The authors list some valid reasons for heterogeneity in estimates between cities, but leave out the two most likely to account for the differences, i.e., differences in particle size distributions and in PM compositions.
- p. 8-7, line 16 Delete “f”.
- p. 8-8, line 26 The AHSMOG papers should be acknowledged here, with a notation that cigarette smoking is not a confounder for this population.
- p. 8-17, Section 8.2.4 The clearest cases for the influence of SES are in the annual mortality cohort studies. WHY WEREN'T THEY CITED HERE?
- p. 8-19, lines 5,6 The Miller et al. (2007b) paper does not fit the statement, and warrants discussion here.

## **Comments from Dr. William Malm**

### Comments on the Visibility Section of Integrated Science Assessment for Particulate Matter, First External Review Draft

The purpose of the draft ISA is to identify, evaluate, and summarize scientific information on the health and welfare effects associated with PM. The ISA is intended to “accurately reflect the latest scientific knowledge useful in indicating the kind and extent of identifiable effects on public health which may be expected from the presence of [a] pollutant in ambient air”

### **Charge to the CASAC PM Panel**

We ask the Panel to focus on the following questions in their review:

- How useful and complete is the scientific evidence presented and summarized in Chapter 9 regarding the effects of atmospheric PM on the environment, including (a) effects on visibility, (b) effects on individual organisms, (c) direct and indirect effects on ecosystems, (d) effects on materials, and (e) effects on climate? To what extent do the discussions and integration of evidence correctly represent and clearly communicate the state of the science?

The focus of this review is on Chapter 9, regarding the effects of atmospheric PM on visibility. To what extent do the discussions and integration of evidence correctly represent and clearly communicate the state of the science?

In general, the section on visibility is well written and by and large reflects the state of the science. However, I have a few comments and corrections, which are summarized below.

#### Section 9.2.1 (Summary of effects on visibility):

Page 9.2: In the second paragraph it is stated that the visibility impairment from each of the major species can be estimated. I would use the word “approximated.” Moreover, the reader is left with the feeling that a certain amount of visibility impairment “is” attributable to each chemical species, which, even if perfect measurements were made with zero uncertainty, is not true. The attribution of chemical species to extinction is an ill-defined problem and cannot in principle be done. However, with certain approximations and assumptions (internal versus external mixtures or assumptions concerning mixing properties of internally mixed aerosols) meaningful apportionments of chemistry to extinction can and are made. There should be some discussion of these issues to demonstrate that EPA has a clear and in-depth understanding of all the issuable scientific questions.

Bottom of page 9.2: What is the Midwest nitrate bulge?

Page 9.3: Why do OC and EC have the highest extinction efficiencies – not because of size or index of refraction but largely because of density differences. Some discussion should be included. Biomass burning is referred to as wild and prescribed fire; there is no mention of agricultural fires.

What is urban excess carbonaceous material?

Comment on how much of the contemporary carbon may be associated with SOA.

Page 9.4: Some additional discussion and emphasis on “sense of well being” studies as they relate to urban visibility. Topics are mentioned on page 9.75 but implications of these studies should be highlighted in the summary section and expanded upon in section 9.3.5.

Page 9.8: Again, agricultural burning is left out of the discussion. It is a clear anthropogenic source of carbonaceous material.

Page 9.10: Nice discussion of night sky visibility. The sentence, “...addition of a light into the sight path, the brightness of the night sky...,” seems to me to be a bit unclear. What is meant by adding a light to a sight path? And why would this be important?

The extinction of starlight is a result of both scattering and absorption.

Page 9.13: Mie theory calculations do not address “particle shape”. Usually, spherical aerosols are assumed; however, more complicated shapes such as cylinders have been used. However, arbitrary shapes are not assumed because calculations are nearly impossible to carry out.

Page 9.15: Replace the reference of Sisler et al. (1996) with Malm et al. (1994).

Page 9.16: Particle size is the most influential property of aerosol with respect to their dry light extinction efficiency. This generally a true statement; however, if one has particles within the accumulation mode, the biggest difference between scattering by, say, sulfate and organics is not generally size but particle density. Ammonium nitrate has a density of 2.3, POM a density of 1.4; that is about a 60% difference in mass scattering efficiency, just due to density!

Page 9.17: Add Malm et al. (2003) to the reference list.

Page 9.19: This figure and associated implications should be incorporated in the monitoring discussion in Chapter 2.

Page 9.20: At the top of page should be  $3.9 \pm 1.5 \text{ m}^2/\text{g}$ .

Page 9.21: Here is the place where a discussion of internal versus external mixtures should be included. The improve algorithm is only an approximation of what is usually an internally mixed aerosol. Furthermore, the main difference between inorganic and organic dry efficiencies is due to assumptions of particle density.

Pages 9.25-9.30: Great discussion of spatial trends. However, the scales are all different, which leads to very misleading interpretations. The scales for each species, at a minimum, between quarters for each species should be the same.

Pages 9.30-9.40: Same issue for comparisons between STN and IMPROVE.

Page 9.35: Differences between STN and IMPROVE samplers should be discussed. STN uses 5 different samplers (Met One, URG, two different R&P instruments, and Anderson), all with different filter sizes and face velocities. These differences result in significantly different monitored OC values for the same ambient OC levels because of volatilization issues associated with SVOCs. Furthermore, STN values, as reported by EPA, are not corrected for positive artifacts effects. How were these issues addressed in the presentations of POM data in Figures 9.19 and 9.20 and in any other figures where STN data are discussed?

Page 9.39: In Figure 9.24 where urban excess is discussed (comparison of IMPROVE to STN), the above issues are critical. Urban excess is interpreted as having its cause associated with emissions, whereas some of the difference may be due to sampling artifacts (blank issues, in particular).

Page 9.41: Trends in haze are very dependent on POM, especially in the West. The episodic nature of wildfire makes it very hard to infer trends of haze. Some discussion of the role of POM in long-term trends especially as it relates to fire should be included here. It is especially critical in the northern Rocky Mountains and the southeastern United States where there are significant emissions associated with prescribed fire.

Page 9.47: Throughout all sections on attribution it would be helpful to have some estimate of uncertainties. I would guess that most of this discussion is semiquantitative at best (bottom of page); certainly, there isn't any difference between 45% and 50%, as is implied in the write up.

Page 9.49: Some cumbersome wording: "However, the Gorge's ..." Consider rewriting. What is the implication of this sentence? So what?

Figure 9.32: On this graph and all others like it, it would be helpful to have labels on each of the pies identifying the pertinent receptor site.

Page 9.51: "track various the organic..." Something is missing.

Page 9.52: It is recognized that current regional models underestimate SOA by significant amounts (see Robinson et al., 2007) for a variety of reasons. One is that source profiles (emission estimates) of SVOCs are severely underestimated, and two, the chemistry in the chemical transport models is very much lacking. Some discussion of these potentially severe model limitations should be presented before modeling results are discussed.

Page 9.57, second paragraph: It should be clearly stated that the estimate discussed here for SOA is clearly a lower bound.

There is considerable discussion on the WRAP weighted emissions potential. This technique needs to be clearly discussed as to what exactly the calculation is and how it should be interpreted. What winds were used in the trajectory calculations? From what heights were the trajectories started? All the assumptions can have significant effects on the results. The reader should be made explicitly aware of the assumptions.

Page 9.71: The fact that sulfate explains 90% of the variance in scattering when sulfate only contributes 64% of the extinction means what? I don't think it means anything more than there are collinearities between sulfate and other species. What is the point of Figure 9.50? The legend for Figure 9.50 is wrong or the graph legend is wrong. I think the legend should read "...particulate nitrate and organic mass..." instead of "...particulate nitrate..."

Page 9.72, bottom of page: "...sulfate concentrations than to changes in nitric acid concentrations..." Not sure what the implications of this statement are. Nitric acid is a precursor to particle formation while sulfate is a secondary aerosol. Would it be more meaningful to talk about SO<sub>2</sub> and nitric acid where SO<sub>2</sub> is the precursor to sulfate aerosol.

Page 9.75: I think the whole discussion on the bottom of page 9.75 should be expanded to present some conclusions of all the studied referenced here, maybe one more paragraph. I think these results are absolutely key to assessing the relevancy of a secondary visibility standard.

Pages 9.78 and 9.79: There are some conversions between variable issues here. For instance, the point is made that all three urban studies have about 20 dv as being acceptable visibility. Yet it is stated that 0.76/km is the median extinction value for Denver's acceptable visibility. Well, 0.76/km is something like 40 dv, not 20. Same issue with the Phoenix study – certainly 45 km and 3.5 km do not correspond to 87 and 12 km visual ranges. The implication that about 20 dv impairment is acceptable at all three locations may not be true.

Page 9.83: \$134 - \$360/what? – day? year?

## REFERENCES

Malm, W. C., Sisler, J. F., Huffman, D., Eldred, R. A., and Cahill, T. A. 1994. Spatial & seasonal trends in particle concentration & optical extinction in the United States. *Journal of*

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

Geophysical Research, 99, 1347-1370.

Malm, W. C., Day, D. E., Kreidenweis, S. M., Collett, J. L., and Lee, T. 5-10-2003. Humidity dependent optical properties of fine particles during the Big Bend Regional Aerosol and Visibility Observational study (BRAVO). *Journal of Geophysical Research-Atmospheres*, 108, art. no. 4279.

Robinson, A. L., Donahue, N. M., Shrivastava, M. K., Weitkamp, E. A., Sage, A. M., Grieshop, A. P., Lane, T. E., Pierce, J. R., and Pandis, S. N. 2007. Rethinking organic aerosols: Semivolatile emissions and photochemical aging. *Science*, 315, 1259-1262.

## Comments from Dr. Robert Phalen

### Chapter 1. Section 1.5 EPA Framework for Causal Determination.

This section presents “a consistent and transparent basis to evaluate the causal nature of air pollution-induced health or environmental effects” (p. 1-11). However, there are some weaknesses. My main concern is that causality might be accepted when it is not true.

1. In section 1.5.2 the statement “An association is prima facie evidence for causation: alone, however...” does not recognize that the **strength** of an association is also a factor that should be considered.
2. In section 1.5.3, page 1-16, lines 4 to 20 discusses the difficulty in dealing with an extraneous factor and in finding “the likely causal pollutant” in mixtures of pollutants. This issue may be a profound one for PM<sub>2.5</sub>, given that evidence for risks for mortality upon long term exposure are found in “eastern and central regions, but not in the western United States” (Zeger et al., *Env. Health Persp.* 116 (12): 1614-1619, 2008). Thus, the likely causal pollutant is not PM<sub>2.5</sub>. Should section 1.5.3 include a requirement that the indicator be valid at all locations before accepting causality?
3. Based on comment #2, should Table 1-2 be modified? Specifically with respect to “Consistency of the observed association”, should consistency among various geographical regions be added as an aspect for judging causality?
4. Also in Table 1-2 under “strength of the observed association” the entry concludes with the statement that “while large effects support causality, modest effects therefore do not preclude it”. It might be good to comment on small effects also, or at least to define how much of an effect is considered to be “large” and “modest”. Are any strengths too small to be used to support causality?

### Chapter 3. Source to Human Exposure

The chapter adequately updates information related to human exposures to PM. There are several undefined acronyms.

1. pg. 3-2, lines 23 & 31: Two main sources of PM<sub>2.5</sub> in the East are initially presented, but the rest of the paragraph doesn't smoothly follow. Perhaps an introductory sentence could explain what this paragraph is about.
2. Table 3.1: Under the column “Accumulation”, some new sources could be added, e.g. wind-blown dust and biological processes.
3. Figure 3.2: “EGUs” should be defined in the caption or on the figure.
4. Section 3.6: Policy Relevant Background might also include excessive levels of resuspended dust on windy days. For example very strong dry wind periods in Southern California are probably capable of producing PM<sub>2.5</sub> exceedences. If any data on such

conditions are available they should be mentioned. This natural problem could lead to excessive regulation of anthropogenic sources of PM<sub>2.5</sub>, which can have serious adverse economic consequences.

5. pg. 3-172, lines 5 to 7: Fugitive dust also contributes to PM<sub>2.5</sub> in the West. This should be added to the paragraph.

#### Chapter 4. Dosimetry

In general the chapter presents an excellent review of the current understanding of inhaled particle dosimetry. The suggestions for improvement are minor.

1. pg. 4-5, lines 16 & 17: Add “and individual genetic variation”, as it is a significant factor in airway morphology.
2. Figures 4-3 and 4-4: In the caption, state whether or not an Inhalability correction was used.
3. Figure 4-5 could be eliminated. The non-natural breathing diminishes its utility, and section 4.2.4.2 treats gender more thoroughly (eg see pg. 4-16, lines 8 to 13. Also, see the admonition on pg. 4-17, lines 26-28.
4. pg. 4-11, line 21: Replace “lower respiratory tract”, which is not clearly defined, with “tracheobronchial and possibly alveolar regions”. This clarification is helpful in view of the predicted and measured increased TB efficiency in small children, which can sometimes decrease alveolar doses.
5. Section 4.2.5: This summary could be eliminated. The preceding sections are sufficient, and the summary has some over simplified conclusions. There are several problems in the Summary, e.g. Inhalability in humans is 77% for a  $d_{ae}$ , not “near 100%” as stated, the carinal enhancements look wrong, etc.
6. Sections 4.3.1, 4.3.1.1 and 4.3.1.2: Two major important factors modifying particle clearance should be added; 1) respiratory tract infections and 2) cough. These factors are strong and widely occur in the population at any given time.
7. pg. 4-23, lines 4 and 5: The last sentence should be dropped. It conflicts with other studies, and the previously-mentioned dog data were for 2 $\mu$ m particles, while the rat data were for 15-20nm and 80nm particles given to intubated ventilated rats.
8. Section 4.3.4.3: The effect of respiratory tract infection on particle clearance is very important and should be added to this section.
9. Section 4.3.5: This summary could be dropped. It is not an adequate summary and it is a bit misleading regarding differences between rats and humans.
10. Section 4.4, pgs 4-32 to 4-36: The terminology is poor. The section begins with “Soluble particles”, which should be replaced with something like “Particles that dissolve rapidly after deposition...”. Good terminology must be established and used for this section and also in Chapter 5. The concept of water-solubility doesn’t work in the respiratory tract. Many substances that are very poorly soluble in pure water rapidly dissolve in the lungs when finely divided.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

11. pg. 4-33, lines 20 to 22: This sentence didn't make logical sense, it should be fixed or dropped.
12. Section 4.4.3: Again, the Summary is very poor. It should be dropped, as it detracts from the quality of the foregoing chapter. Many other chapters do not have summaries, so dropping this one should not be a problem.

#### Chapter 5. Possible Pathways/Modes of Action

1. The word "soluble" is used throughout, see comment 10. above.
2. Section 5.6: It would be helpful to identify the study populations (e.g. human, rat etc.) for each of the effects listed.

#### Chapter 6. Integrated Health Effects of Short-Term PM Exposure

1. Throughout this chapter and Chapter 7, particle measurements are described as "increases" rather than "levels". Increases in levels are not the same as actual levels themselves. Yet, the epidemiology associations based on increases seem to be used by the EPA to set permissible levels of PM. A given increase can occur independently the level of PM. The issue of considering epidemiology associations with "increases" rather than levels should be discussed and justified. I recall a pulmonary physician commenting on this issue during a proposal review session. He indicated that the respiratory tract susceptibility to injury was very changeable and that a few days of exposure to clean air would make it more vulnerable. Perhaps regulating short-term "changes" or "increments" in PM measures (count, mass etc.) would be as good (or better) than regulating low levels. In any case EPA should address the PM "increases" issue. E.g. see pg. 6-10, lines 8 and 9; pg. 6-11, lines 24 and 27; and many places elsewhere. The possible importance of this issue might be seen in section 6.2.10.8 where the results of Villeneuve (2006) differed from the other study results. Also, conclusions based on **increases**, such as that on pg. 6-94 (and other pages) should probably indicate that the conclusions may not apply to **absolute** levels.

## **Comments from Mr. Rich Poirot**

### **Comments on Chapter 9: Ecosystem and Welfare Effects**

#### **General Comments**

This chapter summarizes the policy-relevant science that would support review of and possible revision to the secondary (welfare-based) PM NAAQS. It includes sections on PM effects on visibility, individual organisms, ecosystems, materials, and climate. The section on visibility is substantially more detailed and informative than those on other welfare effects - about the length of the other 4 effects sections combined. I think this emphasis is justified, since it seems unlikely that a secondary PM NAAQS could be an effective mechanism to ameliorate affects of PM on organisms, ecosystems, materials or climate. However the relationships between PM mass (especially PM<sub>2.5</sub>) and/or PM species and visual air quality have been well known for many decades, and a secondary PM NAAQS to protect visibility has been considered in every previous PM NAAQS review - including the original establishment of TSP standards in 1971, when a secondary TSP standard of 150 ug/m<sup>3</sup> was based in part on (minimal) protection of aviation safety (maintaining visual flight rule conditions at airports).

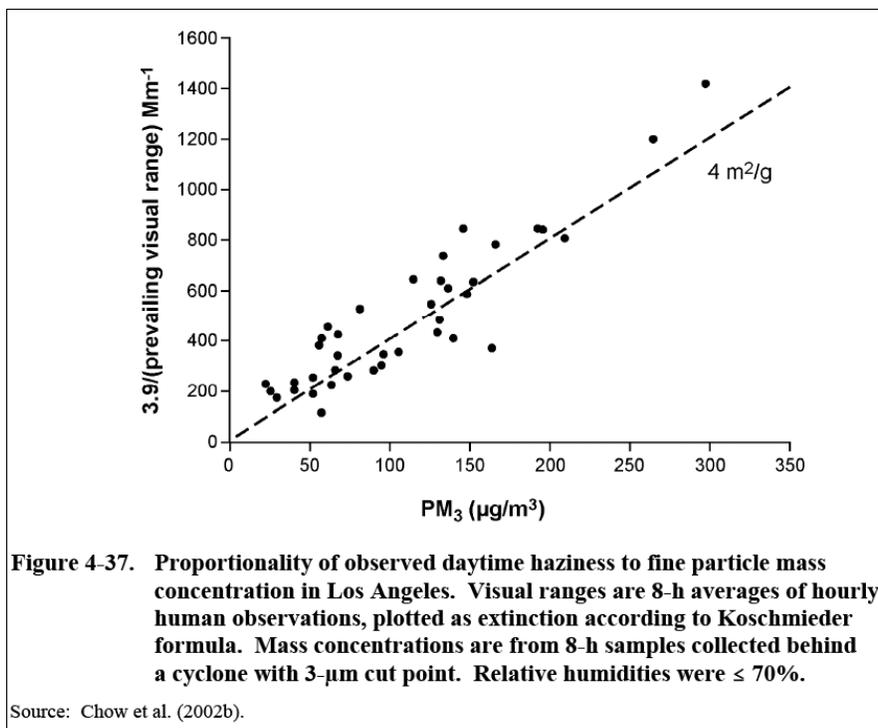
The visibility section of this chapter is clearly written and presents a substantial amount of recent information, much of which has been generated through the work of the Regional Planning Organizations (RPOs), and supporting groups at NPS, EPA, and the IMPROVE program, to help develop the first round of State Implementation Plan (SIP) revisions in response to the 1999 EPA Regional Haze Rule. Consequently, the focus is primarily on effects of individual fine particle species (and coarse particle mass) at remote National Parks and Wilderness Areas.

One general criticism then is that relatively little of the information presented relates directly to causes and effects of visibility-impairing PM in the non-Class-1 rural, suburban and urban areas to which a possible secondary PM NAAQS would apply (although conceivably a secondary PM NAAQS might be exceeded in some of the more polluted Class 1 areas, and could provide added mechanisms to assure improvements in those areas). We would also expect to see improvements in visibility outside Class I areas as an inevitable result of measures to reduce regional haze impacts within them. A secondary PM standard and the Regional Haze Rule need not be mutually exclusive from each other, although it seems useful to think of them as complementary rather than as redundant mechanisms. So it would be useful to see more information focused on the differences between urban/suburban and remote area PM composition and visibility effects.

A second general criticism is that the chapter is predominantly focused on the reconstructed aerosol extinction approach (chemical species measurements combined with generic dry extinction efficiencies and hygroscopic growth functions) which is the basis of the regional haze program. Conceivably, a similar approach might be employed for a secondary PM standard – employing for example the speciation data from the CSN network with a similar or modified “urban” haze equation. However, other approaches might also be considered and the chapter could do a better job supporting those alternate approaches. For example, in reviewing the PM Criteria document in the last review cycle, it was noted by CASAC (Warren White and others)

that an early draft of the PM CD contained no information showing the simple but strong relationship that exists between fine particle mass and visibility (especially under conditions when effects of hygroscopic growth are minimized – such as by focusing on daytime only and/or constrained to hours of lower relative humidity). As a result, the following plot (with associated discussion) was added to the final 2004 PM CD.

**Figure 1. Illustration of Fine Mass / Visibility Relationship from 2004 PM CD**



This graph had earlier been included by Warren White in a JAWMA critical discussion on visibility by Chow et al. (JAWMA 52:973-999, 2002), and attributed in turn to data collected in 1970-71 and published by Samuels et al. in 1973. One point Warren raised was that the strong, linear relationship between fine mass and visibility impairment was well known at the time of the original Clean Air Act. Another point emphasized in that discussion, was that the information provided by detailed, costly, labor-intensive chemical speciation sampling (which currently requires use of intermittent filter sampling over long averaging times) was of value primarily for estimating the effects of aerosol water. A more efficient regulatory approach might take better advantage of current science and technology, by minimizing the importance of water by constraining the averaging time to daytime-only and/or hours with RH < 70% - as has been done in establishing local visibility standards in Denver, Phoenix, Lake Tahoe, etc.

EPA staff and CASAC took a similar approach in recommending a secondary PM<sub>2.5</sub> standard in the last review, based on a daylight-only 4 to 8-hour averaging time (also corresponding more directly to periods when outdoor, sun-illuminated visibility is most important to most people).

An alternative indicator might (if the lawyers allow it) be based more directly on optical measurements, such as by ASOS, transmissometer, nephelometer, or nephelometer + aethelometer (scattering + adsorption). To better support consideration of a fine mass or optical indicators, it would be useful to include some additional attention in the ISA to discuss the characteristics, averaging times, strengths and limitations of various aerosol, optical and meteorological measurement methods; present some illustrative data from urban/suburban areas; and show how effects of water (currently avoided as a component of PM mass), might best be quantified and/or minimized with alternative regulatory options.

### **Specific Comments**

p. 9-2, line 7: Add “by particles” after “scattering”.

p. 9-2, line 8: You might rephrase this to “While a large particle scatters more light than a similarly shaped smaller particle...” or “While a large particles scatter more light than a similar number of similarly shaped smaller particles...”

p. 9-2, line 19: Add “ed” to “call”.

p. 9-3, line 6: Change “and” to “or” or to “and/or”.

p. 9-3, line 16: “Western...”

p. 9-4, line 5: You could add “in rural areas” after “haze”. Note – here and elsewhere in this section, its not always clear whether you’re referring to urban areas or regional-scale (rural) concentrations.

p. 9-4, lines 10-20: Need a reference for this study.

p. 9-4, line 21: You could insert “Perception of” or “The value of” before “urban visibility” to make it clear that you are not referring to urban studies of optics, aerosols, sources, etc.

p. 9-4, line 34 and p. 9-5, line 1: You could delete “, the preferred measure of visibility impairment”, since I don’t think DVs are actually “preferred” by everyone, and also to make it clear that you don’t mean 19 to 25 DV was the preferred measure of impairment....

p. 9-6, line 2: While “N” is correct, I suspect you mean “Ni”. It might also be noted that Zn is an element typically most prevalent in the fine fraction, while V often has a relatively high coarse fraction contribution.

p. 9-7, line 14: Change “is believed” to “is estimated to”.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

p. 9-7, line 16 (or elsewhere): It might be useful to begin with some discussion of EPA staff (& CASAC) recommendations (& policy decisions) from the last PM review. This would help lead to a more “a concise synthesis and evaluation of the most policy-relevant science used to help form the scientific foundation for review of the secondary (welfare-based) NAAQS”

p. 9-7, lines 16 to 18: Since the “recent” information presented here comes quite predominantly from regional haze-related analyses of rural IMPROVE data, I suggest modifying this sentence to: In recent years, most visibility research involved characterizing visibility levels and trends over broad regional scales, improving our understanding of the atmospheric processes and pollutants responsible for the regional impacts, and attributing visibility-impairing pollutants at remote sites to emission sources, source types, and regions.

p. 9-7, line 25 and first 2 lines on p. 9-8: Break this into a few sentences or otherwise fix the grammar.

p. 9-12, line 14: Change “are” to “is”.

p. 9-12, lines 16-17: True, although NO<sub>2</sub> measurement data are often not available, are typically of questionable quality (include other oxidized N species), and may not represent the locations – such as in NO<sub>x</sub> plumes and in layered hazes – where NO<sub>2</sub> effects are most evident.

p. 9-14, line 11: You could change “theoretical” to “Mie theory”, as less sophisticated “theoretical” calculations are certainly possible – and are routinely conducted for the regional haze program.

p. 9-16, line 3: Add “s” to either “term” or “inflate”

p. 9-16, line 21: Add “s” to “aerosol” or add “particles” or “effects” after “aerosol”.

p. 9-18, lines 12-14: Can you provide some quantitative estimates of the underestimation of total extinction due to coarse mode hygroscopic species at Brigantine or elsewhere (i.e. is this important?). Also, if we are concerned with effects of anthropogenic pollutants on extinction, is there any visibility consequence of replacing NaCl with NaNO<sub>3</sub>?

p. 9-18, line 29: Change “are” to “is”.

p. 9-20, line 18: Delete the first “components”.

p. 9-20, lines 19-22: Seems like either too much detail or too little. You could just report the values they recommended, but if you also report the different values they “determined” from their review, then I think additional explanation is needed to justify why they felt compelled to recommend numbers different from what they determined.

p. 9-21, lines 16-23 (or elsewhere nearby): It might be informative to comment here on possible problems in applying this (remote site) equation to urban data – for example, organic mass might be  $< 1.8 * OC$ , and we might also not expect the higher OM concentrations to be well-aged.

p. 9-25, Figure 9-7 (and about the next 20 map figures): The VIEWS system is an excellent tool and these color contour maps are very informative. However, a major limitation has been the lack of user control in selecting the color contour levels. I think the system “auto-scales” these to display maximum information content for each map from the (10) colors employed. This is fine for seeing spatial pattern in an individual map, but makes it difficult to compare maps. I don’t think its critical for this ISA, but it would be useful for many future applications if options were provided for the VIEWS user to specify the contour levels and intervals (i.e. the maximum contour level, number of contour intervals, and ranges of the bins).

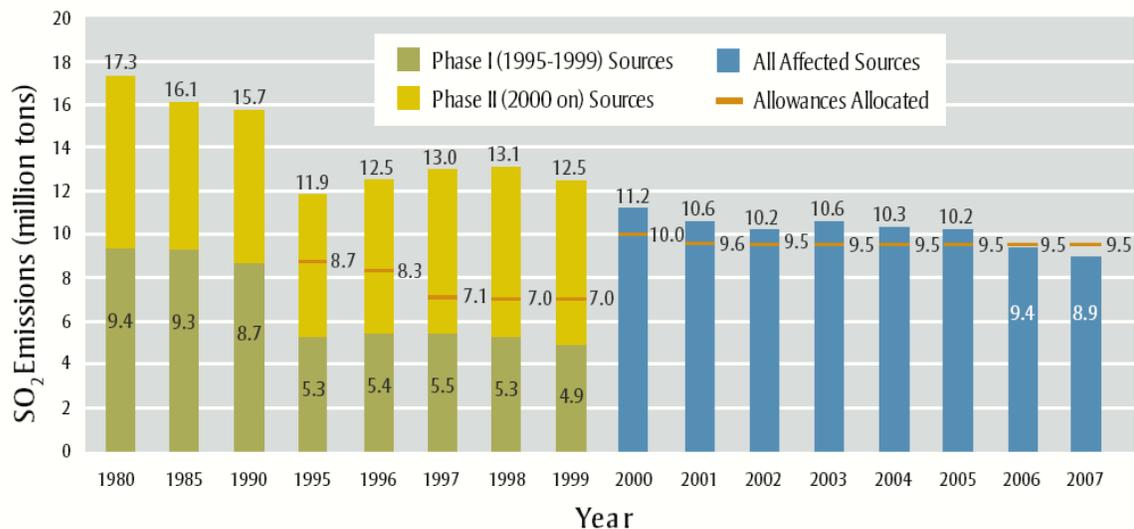
p. 9-27, Figure 9-9, and in text discussion: The Agency has decided that effects of S and N deposition (including particle phase) will be addressed in the review of secondary SO<sub>x</sub> and NO<sub>x</sub> NAAQS and not in this PM NAAQS review, while the secondary aerosol effects of S and N compounds – such as on visibility – will be addressed in the PM NAAQS review, but not in the secondary SO<sub>x</sub> and NO<sub>x</sub> NAAQS review. Since ammonium sulfate and ammonium nitrate have similar dry scattering efficiencies and hygroscopic growth functions and combined account for a majority of visibility impairment over much of the country, it might have been interesting (& still would be) to break out a separate section on (for example include a map here of) the visibility effects of combined S + N aerosols. Such a discussion could be copy-pasted in both the PM and secondary SO<sub>x</sub> & NO<sub>x</sub> ISAs & REAs. A reason for this is that it might help support consideration of SO<sub>x</sub> – NO<sub>x</sub> NAAQS metrics that might have been based on a combined sum of gaseous and aerosol S and N compounds, that might have had (and been justified by) beneficial effects of S & N emissions reductions on both deposition-related and aerosol-related effects.

p. 9-35, lines 8-20 (and following figures): Line 9 indicates that Figures 9-22 and 9-23 show total carbon, but those figures actually show fine soil (the total carbon figures are missing). There needs to be some discussion of the differences in the CSN TOT and IMPROVE TOR carbon methods – indicating that OC & EC don’t have the same meaning at urban & rural sites, although the missing total carbon comparison would be meaningful. Possibly the CSN OC & EC data could be adjusted to make it “IMPROVE-like” before combining it with the IMPROVE data in Figures 9-19 and 9-21 – otherwise I don’t think you should be combining the disparate data. As indicated before, using the same scales for paired IMPROVE and IMPROVE + CSN maps would be helpful. It would also be useful to delete the few urban IMPROVE sites (Washington, Phoenix, Puget Sound, etc.) from the otherwise rural IMPROVE-only maps (if possible).

pp. 9-41, 9-43 (Figures 9-26, 9-27): A discomfoting feature of the haze trends in these figures is that the 10-year period 1995 – 2004 is the period of the Title IV Acid Rain SO<sub>2</sub> emissions reductions in the eastern US. Yet on the cleanest and haziest 20% days respectively, 6 of 14 and 8 of 14 eastern sites show no significant improvement. This doesn’t inspire confidence in successful outcomes of future controls. I suspect this may be partly related to the fact that a large portion of the acid rain SO<sub>2</sub> reductions occurred in the first (1995) year of the Title IV program (and of this trend analysis) and due to spending of banked allowances etc., the actual emissions reductions over the 1995-2004 period have been relatively small. See figure below from EPA “Acid Rain Program 2007 Progress Report” <http://www.epa.gov/airmarkets/progress/arp07.html>.

Possibly some discussion of this “non-trend” could be added here.

Figure 2: SO<sub>2</sub> Emissions from Acid Rain Program Sources

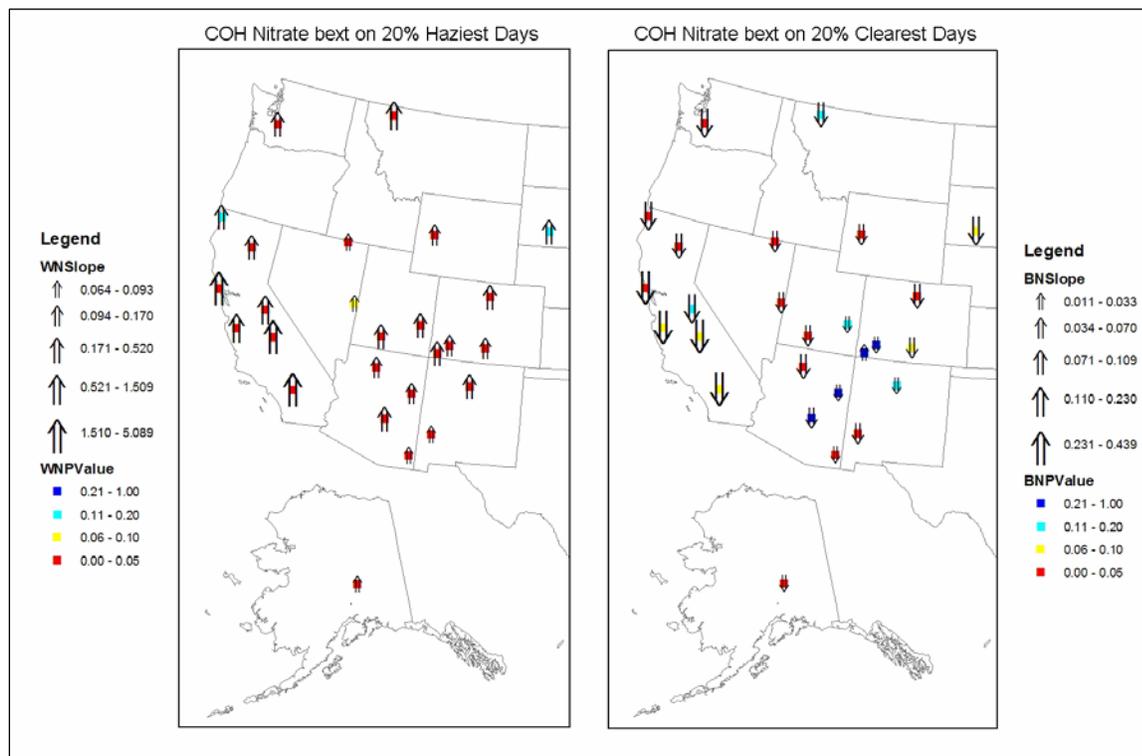


Source: EPA, 2008

p. 9-45, Figure 9-29: Although there are cautionary remarks in the text on p. 9-44 describing this figure, as well as a warning that this “may be misleading” in the figure caption, I’m suspicious of this figure – generated from the “Causes of Haze” website – that shows increasing trends (significantly so at most sites) of ammonium nitrate extinction on the haziest days at all western IMPROVE sites over the period 1994-2003. Extraction of a similar plot from the COH website for the cleanest 20% days shows an opposite trend of decreasing ammonium nitrate extinction on the cleanest 20% days at these sites – and I’m just finding this hard to believe, and suggest double-checking the calculations. If these opposite trends are correct, they would seem to warrant additional exploration (for example doing same for central and eastern sites) and offering some explanation(s) of causality).

**Figure 3. Nitrate Extinction Trends at Western IMPROVE Sites on 20% Haziest Days (left) and 20% Clearest Days (right), 1994-2003 from Causes of Haze Website ( <http://www.coha.dri.edu> )**

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

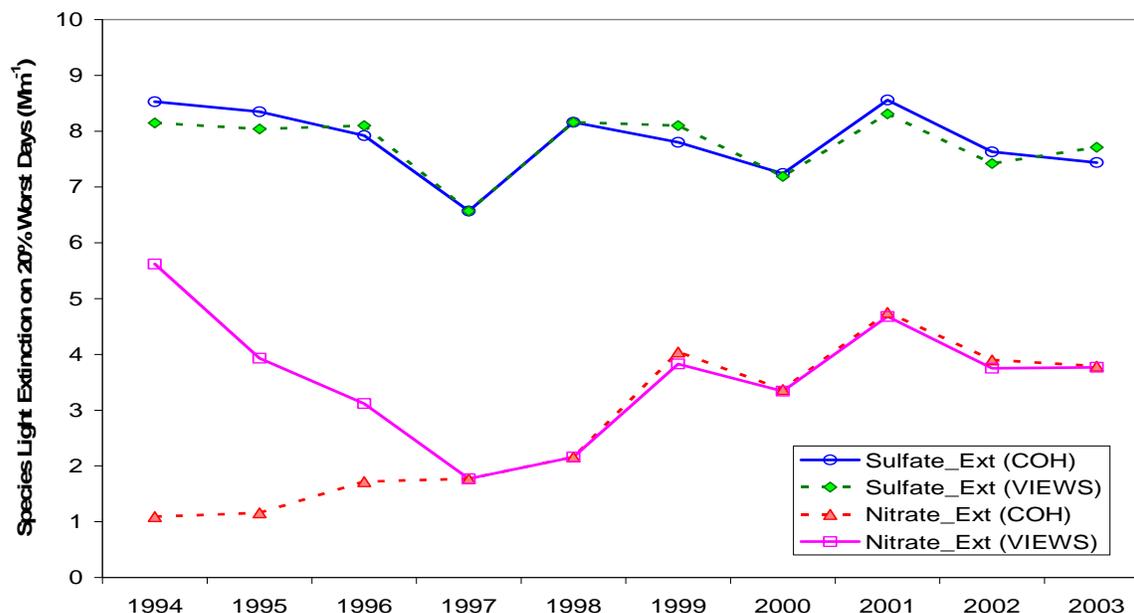


I notice that similar trend information, including estimated extinction calculations on worst 20% & best 20% days by species, site & year can be extracted from both the VIEWS and (for WRAP sites for 1994-2003) the Causes of Haze websites. Comparing the 2 separate sets of calculations (using the RHR1 equation on VIEWS), I note that the results are generally very similar for most species at all sites, but there are substantial differences – especially in the first few years – that seem likely to influence trend calculations, directions and significance levels. I don't know which one is right (if either are), but note they are different. An example of the data for the Lassen Volcanoes NP site is pasted in Figure 4 below.

p. 9-45, lines 1-2: I don't understand what "at any relative humidity" means here. Haze contributions are only proportional to species concentrations at very low humidity. At higher RH, the hygroscopic species contribute proportionately more, relative to their mass fractions.

**Figure 4. Estimated Light Extinction on Worst 20% Days for sulfates and nitrates at Lassen Volcanoes IMPROVE site, 1994-2003, as extracted from the Causes of Haze (COH) and VIEWS websites**

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.



p. 9-46, lines 6,7: Nitrate does not “dominate” in the summer in the Midwest.

p. 9-48, Figure 9-30 and several subsequent figures (9-32 through 9-36). You might add the time periods for which these plotted analysis results apply to the figure captions.

p. 9-57, line 24: Add “s” to “location”.

pp. 9-57 through 9-64: I have a hard time following this discussion and interpreting these figures. A bit more explanation up front would be helpful. Are all these figures really necessary? Also, I note that a large majority (22 of 30 pages) of the discussion and illustrations in this “causes of haze” section 9.3.4.5 pertain to the WRAP RPO region (and to aerosol source apportionment in WRAP class 1 areas only), while only 7 pages are devoted to results from the other four RPO regions combined.

p. 9-74, lines 29-31: While I understand there are some good arguments and strong opinions to the contrary, I don’t concur that the existence of primary health standards necessitates the separation (& removal) of “wellbeing” components (i.e. perceived health effects), from so-called “aesthetic” components when attempting to assess perceived levels of adversity or to evaluate alternative levels at which secondary standards might be set. First, this requires an assumption that the primary standard has in fact been set at a level below which all health effects are prevented. With the TSP primary standard of 260 ug/m<sup>3</sup>, or PM<sub>10</sub> of 150, or PM<sub>2.5</sub> of 65 or 35 ug/m<sup>3</sup>, any observers who perceived health effects at or just below the levels of the primary standard would have been correct, and any regulators who argued that any perceived health effects were irrational and should be discounted at those (health-protective) levels were wrong. Second, there’s a required assumption that its possible to separate a perceived health concern

from the overall emotional response to the visual effects of polluted air. I'm not so sure this is really possible (or necessary), nor do I understand what a purely "aesthetic" response to impaired visibility would mean. Third, I'll argue that there can be a perceived health effect which is different from the actual health effect, but which is nonetheless an important source of stress, malaise, and/or emotional discomfort to the viewer. An analogy would be the strong perception of "unhealthiness" associated with certain "chemical" odors. This perception may occur at ambient concentrations of such chemicals which are not (currently) demonstrated to cause actual health effects. The perceived health effect unavoidably contributes to the perception of a foul, objectionable odor, which adversely affects the quality of life for those exposed to it.

pp. 9-76 - 9-98 (or in a subsequent section): In (or after) summarizing these various urban visibility valuation studies, it might be useful to summarize the urban visibility standards that have resulted in part from some of these studies – or from other public policy decision-making processes (such as for California, statewide and for Lake Tahoe), as well as noting, the scientific and practical reasons for the details of the indicators, averaging times, levels and forms of these standards (such as constraints to daytime-only, and to lower RH levels,...).

It can also be noted that almost all of the preceding discussion was based on results taken from remote, Class 1 areas (which are already "protected" by EPA's Regional Haze Rule. Then there's a jump to "urban" valuation and preference studies, but no mention of such valuation studies in remote Class 1 areas, nor any discussion of visibility effects or valuation in the (non-Class 1, non-urban) suburban and rural areas which compose most (>95%) of the US land area.

p. 9-84, line 2: Since effects of PM (and its precursors and transformation products) on materials are also related to deposition, you might also add a mention of that to this intro on deposition. It might also be appropriate to mention here the PM species for which deposition is of concern for a materials damage or ecological perspective.

p. 9-84, line 25: you might insert "as well as" after "soil," and before "plant" to make it clear that you're not talking about "base cations from soil, plant and insect fragments, ..." etc.

p. 9-85, lines 1-7: This discussion of radiative effects doesn't really belong in the "Forms of Deposition" section, unless you are referring to alteration of radiative effects from reflective snow and ice surfaces as they are modified by deposition of light absorbing particles.

p. 9-89, lines 6-15: I'm surprised we need to go to Italy to find references on primary vs. secondary PM components. Also, I doubt that Cl<sup>-</sup> is really an important secondary PM component in coastal or any other areas. It's predominantly a primary PM component, and often lost from particle phase, prior to deposition. Secondary organics are also important – especially in urban areas. Further, the deposition rates of fine particles are substantially less than for larger particles, such that the dry deposition of particulate matter components in urban areas is likely more heavily influenced by coarse particles, gaseous precursors (or former particle components

that have disassociated from particle phase) than it is by fine particles – even if the fine particle fraction tends to increase during episodes.

p. 9-90, lines 15-16 and Table 9-3 on p. 9-89: Would fit better in the “Mercury” section, 9.4.5.2.

p. 9-98, lines 21-22: Although anthropogenic V is typically heavily enriched in fine particles influenced by oil combustion sources, there can also be substantial concentrations of V in soils, and deposition is likely often dominated by natural sources in some areas.

p. 9-102, lines 1-6: There seem to be some inconsistencies here. For example line 5 describes a global [Hg(0) I presume] reservoir “with a residence time of a couple of years”, while lines 31-32 on p. 9-101 refer to an Hg(0) “residence time of about a year”. Also I doubt that Hg(II) in gas phase has a residence time of “months” or that Hg(II) associated with fine particles has a residence time “similar to Hg(0)” of 1 or 2 years.

p. 9-106, lines 17-18: Its not clear what “much of the burden” refers to. If it resides in the atmosphere, to what organisms is it a burden there? If you’re referring to the “atmospheric burden”, I think pretty much all of it resides either dissolved in fog or clouds or as liquids or solid aerosols.

p. 9-106, line 27: You could add “and other mining activities” after “limestone quarries”.

p. 9-110, lines 1 &2, and generally throughout this section. Sometimes the terms “metals and “heavy metals” are not always used consistently here and sometimes just “trace elements” would be a better term.

p. 9-111, line 3: should be “exposures ...have” or “exposure has”.

p. 9-112, line 9: Change “of” to “to”.

p. 9-113, lines 12-22: I suggest replacing the term “tire dust” with “road dust” in lines 12 14 and 19, and using the term “tire wear” in line 16. For the most part, the dust you’re referring to is not predominantly composed of tire fragments, and its suspension to the ambient air is more driven by the aerodynamic action of moving vehicles rather than the direct action of tires on the road.

p. 9-113, lines 19-22: What’s the meaning of “particles embedded in tire dust”? If Adachi and Tainosho used the term “tire dust”, explain what they meant by the term (how did they collect it?). Is there any explanation for the two different compositions of “brake dust”?

p. 9-132, lines 14-15: I don’t disagree with your assertion that fine mode particles generally have a larger effect on climate than large particles, but I think you need more explanation than “sizes close to the wavelengths of visible light” before proclaiming “therefore...”

p. 9-136, lines 4, 5: This seems inconsistent with your citation to Forster et al., 2007 on p. 9-144 indicating a total direct aerosol RF of  $-0.04 \pm 0.04$ .

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

p. 9-138, Table 9-4 (or elsewhere in this chapter): It would be interesting to see the US subtotals or fractions of the global emissions in this table – or otherwise provide some indications of the extent to which relatively small modulations in the relatively small US contributions to the global aerosol budget might be expected to influence climate.

p. 9-141, lines 1-3: You claim 3 ways but only list 2.

p. 9-142, lines 5-12: The point isn't clear to me here, but I assume any comparison of the effectiveness of reducing BC vs CO<sub>2</sub> or CH<sub>4</sub>, depends on the proportionate size of the reductions in the different pollutants.

p. 9-142, lines 27-30: Not sure what the point is in describing the different assumptions on (internal vs external) aerosol mixtures. Was the range of results -0.39 to -0.78 W/m<sup>2</sup> due to which mixture assumption was used, and if so, which assumption produced the largest result?

p. 9-144, lines 3-10: "These" in the second and third sentences doesn't agree with "Progress" in the first sentence, and you only cite one inter-comparison. I also don't understand why "coarse aerosol fractions are largely responsible for variations in natural emissions". Do you mean "coarse aerosol fractions are largely dependent on variations in natural emissions?"

p. 9-147, Figure 9-57: This is an interesting graphic, but hard to read. I'd like to see it larger with a (much) shorter caption, which refers the reader to the text for a detailed explanation.

p. 9-155, lines 7, 8: Should be "role ... is" or "roles ...are".

## **Comments from Dr. Ted Russell**

### Review of the PM ISA Armistead (Ted) Russell

First, while I am sure I will not be the only one to comment on this, an 800 page document that starts with "... a concise review, ..." might be open to some criticism for what is meant by "concise." I recognize it could be longer, but I also think it could be shorter without losing much in terms of its support of the possible revision of the NAAQS. EPA should resist making the ISA much larger in response to CASAC or other review. My ISA has travelled many thousands of miles to get read. On the other hand, it does pack a lot of information. As to where the document might be trimmed a bit, speaking as an air quality engineer type, there are parts of that section that might be put in an Annex. The main information should be to provide a foundation for understanding the health results later on.

#### Chapter 2

Chapter 2 on the Integrative Health Effects Overview is an important chapter, and reasonably well done. The integrative summary, along with the conclusions, provide a solid and informative overview and highlight the key points. Inclusion of just the causal and likely to be causal relationships make sense because those are what will drive the consideration of revising the primary NAAQS. I would use exactly the same terminology on page 2-11 and in the Tables (I would use causal and likely to be causal). While I like what has been laid out in terms of linkages between PM mass and the health endpoints, I think that the discussion of PM components and sources linkages to health outcomes is insufficient. I would have liked more of a summary similar to what was done for mass linkages, or a statement as to why such is not there. Also, as the Chapter is now 25 pages long, and that this is the chapter that will get read by those not wanting to read the other 800 pages, I think a wrap-up page or two would be called for.

While I like how they have laid out the health endpoints and linkages, I do not believe that the non-health effects endpoints should be left out of this chapter. The ecosystem/welfare endpoints need not get as much attention, but relegating all of that discussion to a single chapter at the end of the ISA sends the wrong impression and might lead one to miss that we are extremely certain about some of the welfare effects. There are some very important effects that are not included in the health assessment (that have possible health impacts via climate modification).

In Chapter 2 (page 2-4) an important point is glossed over: PM<sub>2.5</sub> is a major fraction of PM<sub>10</sub> in many urban areas. This likely drives much of the findings reported here. This is also true at the top of page 2-6 (it is not surprising that PM<sub>10</sub> and PM<sub>2.5</sub> are highly correlated much of the time and in many locations). On page 2-6 they note various methods to measure temporal variation in PM mass and components, but it does not include filter-based techniques anywhere in this section. For completeness, there should be a section just on measurements (one paragraph)

before the discussion of spatial or temporal variability to discuss both integrated and continuous/semi-continuous methods, together. On page 2-7 they state factually that current inventories overestimate primary components etc... the verdict is still out, and more goes in to this than just volatility issues. This comment can be removed from here, though should be discussed in Chapter 3. We are quite unsure of our emission estimates from the various sources, particularly for organic species.

### Chapter 3

Like past ISA's, I like the Source-to-Human Exposure approach to cover that aspect of the review. It is potentially very efficient, though as indicated above, this chapter might be reduced a bit, keeping in mind what the key considerations are later on (e.g., possible mechanisms and their linkage to specific components; spatial and temporal variability and epidemiologic studies; components and epidemiologic results, etc.), and that the chapter will be used for the exposure modeling as part of the risk assessment. I recognize that I might be asking for a bit of clairvoyance to see exactly where the risk assessment might go. The Scope and Methods Documents helped figuring out part of that (see below).

As noted above, one should tread a bit more cautiously about stating that the volatility effects have led to specific under/overestimates in the inventory. This process might be discussed, but there are many other factors that might lead to over/underestimates. (Also, 3-12, 118 is a bit awkward in that the emissions do not estimate anything).

Section 3.7.2.3: This section needs to be expanded (o.k., forget one of my first comments above). Exposure modeling will be key to the Risk Assessment, and either a thorough exposition of the models to be used should be contained here, or such will be required as part of the RA.

Like my comment above, Section 3.8.1.4 should be moved up to be inclusive of all measurement techniques that have been used extensively enough to be included in such a summary (e.g., filter-based techniques). Make a section 3.8.1.2

Section 3.8.2.3 is important and needs to make its points very strongly. It should answer the question (or lay the foundation for answering the question) as to whether confounding is a likely issue just based upon the correlations between pollutants and in the exposure studies. It actually only goes half way. It provides a strong statement about the indoor-outdoor PM source exposure confounding, but not if a gaseous species may lead to confounding. It ends on a negative note that may be of secondary importance (what it says is important in terms of assessing the epi studies for the gaseous species impacts), but not if the gaseous species may confound the PM results. .

Given the issues that have come up in both Scope and Methods documents as to how to treat PM10-2.5, the PM ISA needs to do a more comprehensive job on that topic. The additional information and analysis includes how well it is treated in CMAQ, and the evaluation of CMAQ for simulating PM10-2.5. It also includes how well we can distinguish between the anthropogenic and natural PM10-2.5 fractions, and how the two correlate. Further, given that the SM-Welfare proposes to use scaling of the source apportioned PM2.5 to estimate the corresponding PM10-2.5, the components of that process should be discussed here in greater detail.

Another topic that I worry about from the point of insufficient coverage is climate. While there are many uncertainties as to how aerosols impact climate, there is enough known that this topic should be influencing how we consider revising the secondary standard, and possibly even the primary standard.

Specifics:

Fig 3-1: In the caption, need to do a bit better job as to what the dashed lines versus solid lines mean.

Maps (e.g., Figs 3-19, 21 etc.) A bit more info than just the roads would be helpful (e.g., rivers).

Fig. 3-30. I don't think you mean Pittsburgh in the figure caption. I think it is Philadelphia. Did you mean to switch cities?

Fig. 3-2: Should note anthropogenic.

Page 3-18: Cations and Anions.

Page 3-122: Note sure why they think that the Voyageurs site was not impacted by fires.

Fig. 3-69... Why change colors from prior figures?

Table 3-23: Be consistent in how you distinguish between mod and obs (use mod; obs in the column headings).

## Comments from Dr. Frank Speizer

Pre-Meeting Comments on PM ISA Draft.Oct 2008

Submitted March 25, 2009

Submitted by: Frank E. Speizer

### Chapter 1

General Comment: This chapter outlines both the historical Clean Air Act activities as related to Particles and provides a discussion by which criteria can be applied to establish causality. It seems that after the several iterations that have taken place in trying to get this right, the Staff has put together a summary of the issues that are hard to fault, save one issue mentioned below. . One question might be whether there is a better way to summarize the weight of evidence in terms of consensus building. A recent discussion at the Intergovernmental Panel on Climate Change adopted seven verbal expression of certainty. I list them here for purposes of discussion only to see if CASAC should consider them in our deliberations:

Verbal Description	Percent Certainty
Virtually Certain	Considered more than 99% likely
Very Likely	More than 90%
Likely	More than 66%
More likely than not	More than 50%
Unlikely	Less than 33%
Very Unlikely	Less than 10%
Exceptionally unlikely	Less than 5%

Intergovernmental Panel on Climate Change, 2007

The chapter reads well and needs only minor editing

Added here are the factors in Chapter 1 for causation: (for purposes of discussion)

### **Table 1-3. Weight of evidence for causal determination.**

#### **Health Effects**

#### **Causal**

#### **relationship**

Evidence is sufficient to conclude that there is a causal relationship between relevant pollutant exposures and the health outcome. That is, a positive association has been observed between the pollutant and the outcome in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. Evidence includes, for example, controlled human exposure studies; or observational studies that cannot be explained by plausible alternatives or are supported by other lines of evidence (e.g. animal studies or mode of action information). Evidence includes replicated and consistent high-quality studies by multiple investigators.

#### **Likely to be a causal relationship**

Evidence is sufficient to conclude that a causal relationship is likely to exist between relevant pollutant exposures and health outcome but important uncertainties remain. That is, a positive association has

been observed between the pollutant and the outcome in studies in which chance and bias can be ruled out with reasonable confidence but potential issues remain. For example: a) observational studies show positive associations but copollutant exposures are difficult to address and/or other lines of evidence (controlled human exposure, animal, or mode of action information) are limited or inconsistent; or b) animal evidence from multiple studies, sex, or species is positive but limited or no human data are available. Evidence generally includes replicated and high-quality studies by multiple investigators.

**Suggestive of  
a causal  
relationship**

Evidence is suggestive of a causal relationship between relevant pollutant exposures and the health outcome, but is limited because chance, bias and confounding cannot be ruled out. For example, at least one high-quality study shows a positive association but the results of other studies are inconsistent.

**Inadequate to  
infer a causal  
relationship**

Evidence is inadequate to determine that a causal relationship exists between relevant pollutant exposures and health outcome. The available studies are of insufficient quantity, quality, consistency or statistical power to permit a conclusion regarding the presence or absence of an association between relevant pollutant exposure and the outcome.

**Suggestive of  
no causal  
relationship**

Evidence is suggestive of no causal relationship between relevant pollutant exposures and health outcome. Several adequate studies, covering the full range of levels of exposure that human beings are known to encounter and considering susceptible or vulnerable subpopulations, are mutually consistent in not showing a positive association between exposure and the outcome at any level of exposure.

**Specific Comments:**

Section 1.5, 1.11 Discussion of factors evaluated for causation’, line 28: defines cause, in contrast to statistical association Not clear that this belongs here as part of the discussion. Almost all of the factors entering causation with regard to population data are in fact statistical.

Page 1.15-16: Confounding needs to be defined more clearly, just as effect modification is.

**Chapter 2**

**General Comment:**

This is a useful summary if it indeed truly reflects what is contained in subsequent chapters. There will need to be some cross checking to be sure that the major findings are all summarized here. I would likely take issue with the classification of cancer. I think it will need to be broken down to lung cancer and other cancers as I think the ACS data would at least be “suggestive”.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

#### Specific Comments

Page 2-5, line 13: Assumption is that “diel” is short for diurnal but needs to be spelled out first time.

Page 2-6, end of paragraph at line 23: Suggest a statement is needed here that the composition of PM10 changes by region and that the distribution and ranking as sources of wild fires, road dust and EGUs would vary by region.

Page 2-18, Paragraph on Cardiovascular Morbidity: There is an issue here in that using 1 year data for classifying exposure doesn't make biologic sense for a chronic effect. It needs to be made clearer that the 1 year figures are “surrogates” for long term exposure (over several years).

Page 2-23, Section 2.3.3.: This section coming after the Chronic effects section above needs to be clarified that all the effects assessed in table 2.1 are in fact acute (or semi-acute) effects. Although the table indicates inadequate data for a relationship to cancer there is no discussion in the text. In addition the newer data from ACS would suggest that the classification might be moved up a notch to suggestive.

#### Chapter 3

General Comment: The authors of this chapter have done an exceptional job in summarizing a large body of data and presenting in a readable fashion that makes a very reasonable logical case for the factors that move particles from source to measuring sites, including factors of size, chemistry and transport. Trends over time although not large are impressive. Perhaps more could have been included on the effects of wind direction, although I doubt that much useful data is available that would alter conclusions reached. The last few sections of this chapter that relate to estimates for human exposure and population or community effects are logical and well summarized. I personally would have like to have seen a little more in interpretation of the directionality and factors affecting the directionality of the surrogates used to estimate population exposure. What factors lead to over or underestimation, and perhaps how results might be adjusted for these factors. Perhaps this will come up in later chapters on Dosimetry or Health Effects.

#### Specific Comments:

Page 3-1, line 11: The use of the word “uncontrollable” For describing background pollution level would it not be better to describe this level as “natural occurring”? Uncontrollable could be in the eyes of the beholder, since for some the cost of controlling could predict what was uncontrollable (i.e. Too expensive to control, or technologically difficult).

Page 3-2, last line 34: Some further explanation of the range of values at National Parks is indicated. If the natural occurring background is  $< 1 \mu\text{g}/\text{m}^3$  than what is being defined as background in the range of 3-63 is clearly being impacted by long range transport. This makes for a confusing definition of background. Are we saying that background is natural plus long range transport and therefore varies regionally depending on down wind sources or is background some thing constant, but not achievable?

Page 3-3, line 20: Is it really seasonal differences in sources, or is it differences in photochemical activities by season. One suspects that latter, partly depending upon region where winter heating and summer cooling might result in match emissions from stationary sources and mobile sources between seasons not varying that much and dominate variable being amount of sunlight and temperature.

Page 3-17. Paragraph ending line 15: This section provides well describe logic of what the FRM for PM10 is doing. However, in so doing it provides information that 50% of the particles greater than 10um are getting collected. I think some mention of an “upper limit” needs to be indicated. Is it not the case that there is an absolute cut off at 15 or 30um? And if so (or if not) a justification of what is getting through, particularly when focusing on mass, needs to be offered to deal with the mass not being dominated by these extra large particles.

Page 3-30, Figure 3-4. Need to change monitor indicator from rectangle to circle, if I am reading figure correctly. Ditto figure 3-5.

Page 3-32, Tables 3-3 and 3-4: Need to provide footnote as to why data are “na” for New York City.

Pages 3-40 to 3-46. These pages contain a series of tables and figures that indicate the distributions of PM measures across the 15 sites over the 3 year period. Although the reader can look at these tables and draw their own conclusion, text contained that describes them does not indicate any particular finding. It simply describes what is in the tables. I would have thought that some summaries in text would be appropriate (like the 75%tile are all above the annual standards or although some values exceed 1000 ug/m<sup>3</sup> at the max, the 95%tile do not ever exceed 60ug/m<sup>3</sup> for the 3 years 2005-2007 or Phoenix and Denver are the only cities with PM10-2.5 with annual means 20 or higher, etc). See text descriptions on pages 3-51-3-53 for Figures 3-9-3-13 which give a much better assessment of what is presented.

.Page 3-87, Figure 3-42. The text indicates that this figure is to be replaced. I look forward to seeing the replacement, particularly because this figure and the accompanying text to my mind is critical to our understanding of the effects of distance from source, particularly as related to road traffic for ultra-fine particles.

Page 3-109, Figure 3-58. Typo in Vertical Axis.

Page 3-130, Figure 3-70. Should this be divided into two figures (if data exist) since there is a real mixing of children, who contribute almost all of the in school time, with adults who are more likely to be out and about or indoors in a different setting?

Page 3-132, after line 5: A further conclusion here would be useful. If ambient concentration is better than personal exposure as a surrogate for ambient exposure is ambient exposure less likely

to over or underestimate true exposure. Maybe this will come up in the next section, but with the relatively high correlations in table 3-27 some statement is necessary.

ADDED note after page 3-160. This section is well written and summarizes well the issues needed to be considered. However, I would still like to see a more interpretive statement of the bottom line. Do ambient measures over or underestimate population human exposure and if so in what direction and under what circumstances or what influences the direction of the over or under estimation?

Page 3-168, line 7: Is this last sentence true for all regions? I would have thought that broadly in the Midwest or western plains we know more about PM10-2.5 as indicated in some of the tables.

## Chapter 5

### General Comment:

This chapter presents a number of mechanisms of injury but does not appear to be presented in an even fashion. In some cases the mechanism is being discussed from a basic pathophysiologic perspective with no particular relation to PM exposure, in others it is more focused on the effects of PM. I think this is ok, since in the next chapter it has been promised that the focus will be on PM. This might be helped by some cross referencing on the last 2 pages where there are a number of bullets (some of which could be combined) with added references to places in Chapter 6 and 7 where they are discussed. One issue that seems to be missing (and may be missing from the subsequent chapters) related to potential reproductive outcomes. Although there is not a lot of data there are several studies pointing in this direction so potential mechanisms probably should be considered.

## Chapter 6

### General Comments:

Reasonably well done job of integrating toxicology, human studies and epidemiology for each of the exposure scenarios discussed as well as for each of the outcomes of interest. However, the text gets overwhelming when it gets to the summaries. The initial parts of presenting the level of causal certainty is fine, but then the details provided on the various disciplines data (epi, human clinical, and tox) seem to get somewhat contradictory. For example, the discussion of short term respiratory morbidity general conclusion seems to be contradicted with discussions of specific symptoms or pulmonary function, which does apply to all groups equally. Surely that is not the place to be bringing out the subgroup variation, unless the purpose is to confuse the reader. It is also quite redundant as all of the details are previously discussed in the chapter. I would have left more of the toxicological studies in the appendix only.

### Specific Comments

Page 6.3, paragraph beginning line 11: This is an appropriate discussion of time-series, but somewhere in the paragraph it needs to be stated more explicitly that there is generally a relationship between PM and mortality that is seen in these studies. Then it becomes appropriate to discuss the statistical issues and issues of threshold

Page 6-4, line 23: Should this be “linear **non-threshold**”?

Page 6.7, line 11: Subtle, but would change “do” to “may”

Page 6-18, line 30: The reason one expects a decline in HRV with exposure is because of the Framingham data that suggests lower HRV predicts CVD. However, there are some who suggest that change in HRV in either direction represents a response. See top of page 6-21 on animal studies. It therefore may not be appropriate to call the response “inconsistent”.

Page 6.24, line 11: typo; ditto line 12

Page 6.28, line 5: “discrepancy” is a value judgment that would appear unnecessary. I would suggest something like variability in the several studies.

Page 6-54, lines 12 and 14: Please check whether **100ug/m3** is correct. (Would have thought it should be 10ug/m3.)

Page 6.85, line 19: Issue with the word “consistent” In fact looking at figure 6.2 the results is really quite consistent. All but one show a positive effect, albeit that not all are statistically significant. With the subsequent data on heart failure admissions and ER visits it I suspect the summary could be a little more positive than as expressed.

Page 6.88, line 23: I would agree with the conclusion as written but it begs the question of what is the summary of the ambulatory arrhythmia data. Will this come up later? If so probably should indicate to be discussed in section 6? If not should be discussed here.

Page 6.90, line 27 end of summary. There is a particular issue with regard to stroke. Some comment need to be made that the appropriate lag structure is simply not known. The 0-2 days may not be appropriate as the onset of symptoms may be much longer than is reflected in administrative data bases on date of admission. Most of the studies cited do not include any specific query about symptom onset. This is particularly true for the embolic disease which make up about 80+% of the events and in which the events are likely to be acute than for the hemorrhagic strokes.

PAGE 6.94 SUMMARY: Logic well presented with discussion of toxicological data to support mechanisms for the conclusion of **likely causal**.

6.94, line 26 to end of 6.96: this section seems out of place. It is a summary of the details used in the second paragraph on page 6.94 and therefore might all come before the last paragraph on page 6.94 (which is the conclusion for the section on PM10).

Ditto next several sections.

Page 6.93, Section 6.2.11 Summary and Conclusions

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

<u>Pollutant</u>	<u>Chapt statement</u>	<u>Reviewer position</u>
PM10	Likely causal	agree
PM2.5	Causal	agret
PM10-2.5	Inadequate evidence	+/- agree
Ultrafine	Inadequate evidence	agree

Because PM2.5 is contained in PM10 and particularly because PM10-2.5 in inadequate some discussion need to be here as to what the evidence is that makes PM10 likely causal **separate from** effects of PM2.5. Even is the argument is that for many of the studies it is the only data we have. Further at least for Ultrafine, (and perhaps for PM10-2.5 it needs to be stressed that it is the lack of sufficient study rather than either inconsistent studies or clearly negative studies.

#### Respiratory effects

Figure 6.5 and 6.6 and Table 6.7: Although all the information is in these figures and table, (and is given in the text) it is somewhat frustrating in that I would like to see the odds ratios along side the pollution measures. How to do this? Maybe it is done in the Appendix and I will check. If there however, a cross reference is necessary. If not, it probably ought to be there.

Page 6.117, lines 18-22: Potential problem in that the mass data for PM<sub>2.5-01</sub> contains all of the count data NC<sub>01-1</sub>. Therefore the attenuation would be expected. This is hinted at in the statement that the correlations with the gasses is high but probably needs to be better spelled out.

Page 6.124, line 2: typo; ditto page 6.134, line 4

Page 6.152, line 5-6. The entire tox section (now that it is written) probably could have been a lot shorter. It reads too much like the old CD, and the writer could have been asked to shorten. As indicated here much of the tox material presented was done at high doses. And thus is less relevant and therefore relegated to the appendix. .

Figures 6.9-6.11. I find it useful in these figures to have provided the range of estimates from the 2004 CD. However, in presenting these individual and multicity studies for the most part there is an overlap with 1 as presented? I assume there will be a combined risk assessment analysis presented in subsequent document but it would be useful to have it here as well.

Several of the figures: May want to put into the legend of these figures that they are expressed as Excess Risk % (if that is what they are)!

Page 6.182, line 8. This sentence needs to be qualified. It appears to apply only to asthmatics and the elderly.

#### Summary and Conclusions

<u>Pollutant</u>	<u>Chapt statement</u>	<u>Reviewer position</u>
PM10	Short term Respiratory Morbidity	likely causal agree
PM10-2.5	Short term Respiratory Morbidity	suggestive of causal agree

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

PM2.5	Short term Respiratory Morbidity	likely causal	causal
Ultrafine	Short term Respiratory Morbidity	inadequate evidence	+/- agree
PM	CNS Symptoms or Disease	inadequate evidence	agree
PM10	Short term mortality	likely causal	agree
PM2.5	Short term mortality	likely causal	causal
PM10-2.5	Short term mortality	suggestive of causal*	+/- agree
Ultrafine	Short term mortality	inadequate evidence	agree

\* Might take issue with fact that although fewer studies, with regard to cardiovascular disease the measure of PM10-2.5 appear to be where PM2.5 were in 2004 and might move up to likely causal with a few more studies. (not likely to go the other way).

Page 6.247, Table 6.16 starting this page

I do not find this a very useful table as a summary of Epidemiologic Studies for source apportionment. First many of the studies reported are not epidemiology (e.g. the first one is mice). Second there is lots of NR or na reported in the table. I do not get the message from the table. Suggest reduce more specifically or leave out.

## Chapter 7

General Comments: There are several difficulties with the way results are presented in this chapter. First of all most of the contrasts in exposure that are discussed are presented as increases in pollution when in fact they are not increases but differences between regions. Secondly and perhaps more important results are reported as differences in hazard ratios or rates, albeit mostly with c.v.s given, that can only be described as null effects. This is carried throughout the presentation of the individual outcomes. In particular this relates to intermediate outcomes related to CVDs. In fairness generally there is a summary statement at the end of the section that indicates the author recognizes this but it needs to be part of the description of the results rather than what appears to be a pushing of the results. To anticipate what is coming it might also be discussed as to the role of these intermediate outcomes in the process of identifying health outcomes. If anything there is a prior that is mentioned early on that chronic inflammation is a major pathogenesis pathway. In fact since the markers used for estimating this effect are not related to air pollution, it suggests that some other alternative mechanisms should be invoked.

### Specific Comments:

Page 7.1, line 1: Minor point. Should the order be changed in this sentence?. The chapter reviews, integrates, and summarizes rather than summarizes first.

Page 7.2, line 12: I am not sure that all would agree with this. Chronic inflammation may be a component of Atherosclerosis but certainly is not the sole cause.

Page 7.2, line 24: Define CAC if first time used.

Page 7.2-7.3: Although useful to define the clinical tools used to assess atherosclerosis, what is missing is the any quantitative assessment of the coefficient of variation of these tools. This is particularly important since the next sections indicates small differences resulting from deltas in PM of 10ug/m<sup>3</sup>..

Page 7.4, two paragraphs. There is something terribly wrong between these two paragraphs. The magnitudes of the deltas in the first paragraph are virtually zero and none are significant. To discuss them as “increases” is ludicrous. On the other hand deltas in the second paragraph are 50 to 100 times higher and are significant, albeit the PM measures are different. Is there a decimal point error in one or the other?

All of the epidemiology section on Atherosclerosis: This entire section needs to be rewritten. Except for the one study from Germany all of the other data presented is definitely null. To describe any of the findings as showing “increases” “associations” etc. is misleading the reader. In addition, since these are cross sectional studies to describe differences in PM levels as increases in also not correct.

Page 7.9, line 13: change “increase” to “difference”

Page 7.15, line 13: again change increase to difference

SAME PAGE, In line 15-16 in contrast to lines 13-14 is the reference to NON-FATAL CHD or MI? Otherwise these are two opposite statements about PM<sub>10</sub>. Alternatively, one statement may be about PM<sub>10</sub> and other PM<sub>2.5</sub>. Please check.

Line 23, again change increase to difference

Page 7.17, line 6: ditto

Line 13-15: Two problems. What does it mean after adjusting for clinical characteristics to not find a prevalent difference in CHD? If one of the clinical characteristics is prevalence of disease this is what would be expected. Second the deltas reported with the c.v. given are really null. To describe them as difference is misleading.

Line 21: Again, these findings are null. (Alternatively to be consistent with the way others are being reported one would say that a 10ug/m<sup>3</sup> difference in PM was protective!

Lines 28-29: What does this mean given the previous sentences reflects a null?

Page 7.18, line 20: Don't need OR and % difference. (They are the same numbers)

Page 7.21, line 4-5: This conclusion needs to be revisited. Most the studies reported are in fact null, albeit that they are in the direction that might lead to this conclusion. The important issue is that the direction of the effects is supported by the toxicological work. This needs to be factored in, somehow, to the logic that allows the author to reach this conclusion.

Page 7.32, Figure 7.4 As presented this figure is more confusing than enlightening. It mixes up both cross sectional effects with longitudinal change. It is not clear what arrows going in both

directions means. The text that describes some of the finding is much clearer. I would recommend leaving Figure out or expanding greatly and perhaps even making it into multiple figures.

Page 7.33, sentence beginning line 1. Not clear what is meant by pulmonary function in first year of life, surely not the measure reported.

Paragraph beginning line 16. Not clear how exposure in 1<sup>st</sup> and 2<sup>nd</sup> trimester is separated from 3<sup>rd</sup> trimester.

Summary results

<u>Pollutant</u>	<u>Chapt statement</u>	<u>Reviewer position</u>
PM10	Long term CVD morbidity	suggestive of causal agree
PM2.5	Long term CVD morbidity	likely causal agree
PM10-2.5	Long term CVD morbidity	inadequate evidence for yes or no agree
Ultrafine	Long term CVD morbidity	inadequate evidence for yes or no agree
PM10	Long term Respir Morbidity	likely causal agree
PM10-2.5	Long term Respir Morbidity	No data for conclusion on causality +/-agree
PM2.5	Long term Respir Morbidity	likely causal causal
Ultrafine	Long term Respir Morbidity	inadequate evidence suggestive

Section 7.4.2 Toxicology of reproductive outcomes. Much of this could have shortened or left to the appendix. As indicated before this section none of the mechanisms seem applicable to the epidemiologic findings. Therefore it seems the details of the toxicological data are not really helpful and just makes the chapter too long.

<u>Pollutant</u>	<u>Chapt statement</u>	<u>Reviewer position</u>
PM10	Reproduct & Developmental	suggestive of causal agree
PM10-2.5	Reproduct.& Developmental	inadequate evidence agree
PM2.5	Reproduct & Developmental	suggestive of causal agree
Ultrafine	Reproduct & Developmental	No data for conclusion on causality agree

Section on Cancer: This section is extremely disappointing with regard to the presentation of the epidemiologic data. The author seems much more comfortable presenting a discussion of the toxicology, carcinogenesis and mutagenesis even to the point of discussing in vitro studies. The epi is extremely naive. For example, on Page 7.87-88, Paragraph on Breast Ca and TSP: These data are presented in a crude fashion with out discussion of possible confounders. The ORs are in fact considerable higher than any reported with smoking, where the exposures to potentially toxic agents are considerably higher than might be seen from environmental TSP. A more careful reporting therefore is warranted. Further there is no discussion of any other studies. This appears to leave out the Pope analyses of the Amer Cancer Society study, which does indicate a rather well confirmed risk about a 40% excess risk of total cancer with higher risks for lung cancer.

I would therefore disagree with the summary of inadequate data for an estimate of causality. I would suggest at least suggestive.

Page 7.117, sentence beginning line 7: This needs to be reworded. The fact that the new studies focused on CVD effects rather than respiratory effects doesn't make the respiratory effects any less important (except there are less of them). I think the authors know this but the way they have said it reads as though a change in thinking has occurred. This will come up again in next chapter.

<u>Pollutant</u>	<u>Chapt statement</u>		<u>Reviewer position</u>
PM10	Overall Chronic mortality	suggestive of causal*	likely
PM2.5	Overall Chronic mortality	likely causal	agree
PM10-2.5	Overall Chronic mortality	inadequate evidence	+/- agree
Ultrfine	Overall Chronic mortality	not considered	suggestive

\*Might be argued that there are sufficient evidence to raise to likely

## Chapter 8

### General Comment:

The authors have effectively laid out the potential susceptibility and vulnerability characteristics and then systematically discussed each. One might take issue with the conclusions that almost in every case because there is some inconsistency in the results reviewed that the uncertainty that results leads to the position that more research is needed. Albeit it true that should not leave the document without indicating more or less to what degree the argument is made. In fact in most cases the reasons the particular characteristic is on the list is because there are some groups in which there is more than chance operating that a particular subgroup is more susceptible or more vulnerable. Chapter needs a concluding summary paragraph.

### Specific Comments:

8.14, line 5: This statement may be true for "in association with exposure to PM" but is not true as stated in general. Clearly those with COPD are more susceptible to exacerbations of COPD. Suggest qualify sentence more specifically.

## Comments from Dr. Helen Suh

### Integrated Science Assessment for Particulate Matter (1<sup>st</sup> External Review Draft) Comments

Helen H. Suh  
Associate Professor  
Harvard School of Public Health  
Boston, MA 02215

March 25, 2009

**Question 1:** *The framework for causal determination and judging the overall weight of evidence is presented in Chapter 1. Is this framework appropriately applied for this PM ISA? How might the application of the framework be improved for PM effects?*

The two-step framework for causal determination and weight of evidence is sound and is appropriately adapted to PM by allowing this framework to be applied separately for different sized particles (PM<sub>10</sub>, PM<sub>10-2.5</sub>, PM<sub>2.5</sub>, and ultra-fine particles), different adverse health/welfare outcomes, and short and long-term exposure periods. Although implicit to this framework, the explicit consideration of causality by major particle sources or components should also be considered, even though there is currently insufficient evidence to make any determinations. In addition, there should be some integration of evidence across particle sizes as well, especially given that PM<sub>10</sub> includes PM<sub>2.5</sub>, PM<sub>10-2.5</sub>, and ultrafine particles and that many recent health studies (especially of intermediate health markers) no longer examine PM<sub>10</sub> by itself. In this regard, it may be preferable to include discussion and consideration of PM<sub>10</sub> after that for PM<sub>2.5</sub> and PM<sub>10-2.5</sub>, with findings used as evidence in support of or contrary to those for PM<sub>2.5</sub> and PM<sub>10-2.5</sub>. Else, causal determinations for PM<sub>10</sub> should be made in part based on determinations for PM<sub>2.5</sub> and PM<sub>10-2.5</sub>. This reorganization may help to explain apparent inconsistencies in causal determinations (as discussed further below).

**Question 3:** *To what extent are the atmospheric chemistry and air quality characterizations clearly communicated, appropriately characterized, and relevant to the review of the PM NAAQS? Does the information on atmospheric sciences and exposure provide useful context and insights for the evaluation of human health effects of PM in the ISA?*

a. *Is accurate and appropriate information provided regarding PM source characteristics, techniques for measuring PM and its components policy-relevant background PM, and spatial and temporal patterns of PM concentration? Are the analyses and figures presented in Chapter 3 effective in depicting ambient PM characteristics?*

Chapter 3 presents PM composition, sources, and spatial and temporal trends for PM, its associated size fractions and its major components in a clear, concise, and well organized manner, with trends shown for different spatial (neighborhood, urban, regional and global) and temporal (hourly, daily, and yearly). Specific comments are below:

- For clarity all figures and tables should explicitly state the averaging time of the measured concentrations.
  - As was done for PM<sub>10</sub> and PM<sub>2.5</sub>, maps illustrating the location of speciation monitors relative to population density should be included, although perhaps just in Annex A.
  - A table showing a summary of the exposure-related factors for each of the selected 15 cities should be added. These factors may include population density, number of large stationary PM sources, some metric of traffic congestion, percent of population living within 100 meters of a busy road (e.g., class A1 or A2), percent of people living in apartments or single family homes, and central or room AC prevalence.
  - The Figures 3-14 through 3-18 were very informative and effectively showed the variation in PM<sub>2.5</sub> composition by region and by season; it would be helpful to have the sample sizes noted somehow as it would help determine the comparability and robustness of the city-to-city comparisons. The discussion of how composition may vary within a city and near sources should be expanded.
  - Although noted, interpretation and discussion of Figure 3-43 should emphasize that even though neighborhood scale variability in PM<sub>2.5</sub> was rather low, it may not be the case for PM<sub>2.5</sub> components, as concentrations of locally generated components, such as EC, have been shown to vary substantially over very short distances.
  - Diurnal variation in hourly EC, OC, SO<sub>4</sub><sup>2-</sup> and other major particle components should also be presented and discussed, especially in relation to particle number concentrations.
  - It would be interesting to include some discussion or graphic of sites that are in violation of the annual but not 24-h NAAQS for PM<sub>10</sub> and PM<sub>2.5</sub>, specifically related to whether these sites exhibit a seasonal or spatial daily concentration pattern.
  - Although introduced in Section 3.5.1.3 and discussed later in 3.7.2.3, methods used in source proximity studies, such as land use regression models, should be mentioned in the section *Estimating Source Contributions to PM* (Section 3.5.4)
- b. *Is the evidence relating human exposure to ambient PM and errors associated with PM exposure assessment presented clearly, succinctly, and accurately? Are there PM exposure issues that should be expanded, shortened, added or removed?*

While relatively complete, this section is generally not as cohesive and clear as the previous section. It would benefit from an upfront section that briefly introduces the concept of exposure, its relation to ambient levels, and its importance in the interpretation of ambient concentrations and health risks. This introduction could then be followed by a brief description of the sections or discussions to follow. In addition, for consistency it would be preferable for this section to follow the pattern established in other parts of the ISA, with each topic discussed for each PM size fraction (e.g., PM<sub>2.5</sub>, PM<sub>10-2.5</sub>, PM<sub>10</sub>, ultra-fine particles, and components) and also for acute

and chronic averaging periods. As currently written, the sections jump between PM measures quite a bit, with the specific PM size fraction often not mentioned (although assumed to be PM<sub>2.5</sub>). Alternatively, the exposure section could follow the general structure of the Human Exposure section in the Conclusions (Section 3.8.2), which is very clear, well written, thoughtful and concise.

Specific comments are below:

- Page 3-131, lines 7-3-132 is too complicated, long, and confusing. Its main points are important, making their clear and simple discussion even more necessary. It is possible that this section is misplaced, adding to the confusion.
  - Section 3.7.2.3 *PM Exposure Modeling* should include a discussion of time-weighted microenvironmental models and GIS-based spatial smoothing models.
  - The section entitled “Outdoor Exposure to Local Sources” is misplaced and should be moved to Section 3.5.4.
  - Figures 3-74 and 3-75 should be clearly annotated with regard to the location, study population, and time period of the study
  - Section 3.7.4 *Exposure Assessment and Socioeconomic Status* is misplaced and should be moved to the Section 3.4.2.2.
- c. *To what extent does the Panel find Annex A appropriate, adequate, and effective in supporting the ISA?*

Annex A contains a voluminous amount of data, which takes away somewhat from its effectiveness. Further, several figures and tables are contained in both the ISA and in the Annex, probably mistakenly, but they should only appear in only one place. Regardless, the Annex adds important, supporting concentration and exposure information to the ISA. Figures that could be condensed into tabular form include:

- city-specific maps of monitoring site by population density and SES, which while beautiful are numerous; data could be placed into a single table each for the PM<sub>10</sub>, PM<sub>2.5</sub> and speciation monitors.
- city-specific PM<sub>2.5</sub> composition pie charts, with data expressed in the table as a range if there are multiple pie charts for a given city

To help sort through the data, it may also be important to categorize findings further. For example, studies summarized in Section A.4.1 *Exposure Assessment Study Findings* should be grouped first by general topic area and then sorted alphabetically by last name of the first author.

**Question 7:** *Strength, consistency, coherence, and plausibility of evidence for health effects of PM?*

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

The causal determinations for the various PM measures are appropriate and supported by the available scientific evidence. Some allowance may be necessary for determinations of causality for PM<sub>10</sub> either now or in the future, as an increasing number of health studies appear to no longer examine the health risks associated with ambient PM<sub>10</sub>. As a result, additional evidence of PM<sub>10</sub>-associated acute or chronic health impacts may be difficult to obtain or may have to be pieced together from PM<sub>2.5</sub> and PM<sub>10-2.5</sub>.

As mentioned above, causal determinations for PM<sub>10</sub> are not always the same as those for its size fraction groups, PM<sub>2.5</sub> and PM<sub>10-2.5</sub>, which can present seeming inconsistencies. For example, if short term effects of PM<sub>2.5</sub> are causal with relation to cardiovascular morbidity, why isn't the same determination made for PM<sub>10</sub> given that (1) PM<sub>2.5</sub> generally comprises a substantial fraction of PM<sub>10</sub> and (2) correlations between 24-h ambient PM<sub>10</sub> and PM<sub>2.5</sub> tend to be strong. The practical implications of this and other seeming inconsistencies should be noted.

## Comments from Dr. Sverre Vedal

### PM ISA 1<sup>st</sup> draft

April 1, 2009

reviewer: Sverre Vedal

For each chapter, numbered points that are considered to be more major, general or substantial are followed by a subsection of more specific points.

### Chapter 1. Introduction.

1. Organization. The flow of topics is generally good, but there are some places where consolidation and change in ordering might help.

Examples:

1-15, line 21. This starts the discussion of confounding, but this is continued and completed only later (line 33 and p. 1-16) after it is interrupted by bringing up the notion of effect modification. Line 25 starts a listing of the “multiple ways” PM can be associated with outcomes, but only lists three ways. There are other ways of getting a spurious association: e.g., any number of non-pollutant factors that are associated either in space or time (depending on the study design) with PM. [By the way, I’m not sure effect modification has a place in a discussion of causation. Also, the definition of effect modification here is awkward and weird - effect modification simply means that exposure effects differ across some subgroups or strata of the population.]

1-16, line 32. The measurement error discussion here should follow immediately after the multi-pollutant modeling discussion (line 11, etc.), rather than being interrupted by a discussion of stratified analysis.

2. Causality criteria and grades (Table 1-3).

i. Although the Hill criteria probably need to be brought up, they have limited utility, as evidenced by all of the qualifiers in the description of each criterion. The desire to avoid “criteria” is understandable, but replacement with “aspects” (1-18, line 8) is awkward – how about “characteristics”? “corollaries”?

ii. The weight of evidence grades (1-22) are problematic. Some suggestions: 1) drop “reasonable” as a qualifier to confidence for the causal grade – “reasonable” to me is not strong enough to allow a categorization of causal; 2) I’m not sure I see much difference between “likely” and “suggestive” here; 3) why is there no “not causal” or “likely not causal” category vs. “suggestive” of not causal only? i.e., there is no symmetry here. In general, I don’t think there’s much to be gained by trying to make these grades parallel the 5-level categories of EPA Guidelines for Carcinogen Risk Assessment (footnote 1-21).

iii. See 3.ii, below.

3. Things not discussed.

- i. It is important in this chapter to bring up publication bias: how it happens, the evidence for it, its impact on both the assessment of causality and the exposure-response relationship (slope and shape), and how it's countered.
- ii. There are also other soft criteria that have been floated recently (e.g., the Ioannidis series of papers) that highlight features influencing whether published findings turn out to be true; these could bear on our assessment of the published scientific literature (i.e., the literature being evaluated here) and the determination of causality. A few points that should increase suspicion and vigilance: small effects sizes, large number of potential comparisons, flexibility in outcomes and modes of analysis, potential for conflict of interest, a "hot" scientific field. I bring this up with some hesitation, but decided in favor of it when I again noted the many instances in the air pollution health effects literature where this perspective might have merit.
- iii. What is the solution? Replication of specific findings is important and should be heavily weighted. To avoid selective reporting of positive findings, an attempt should be made to report and compare all findings (all exposure periods and lags, all endpoints, all subgroups, etc.), although this is admittedly a tall order.

#### Specific.

- 1-12, line 17. It is not clear that the type of important evidence would vary by pollutant – it would if this were based on the availability of evidence for different pollutants, but I would think the important evidence should be pretty much the same.
- 1-12, line 23. Sometimes there can be an intervention in observational studies: e.g., vitamin interventions with ozone, or fish oil with PM.
- 1-12, line 29. Toxicology studies are also useful in enhancing plausibility of exposure effects.
- 1-13, line 7. The definition of counterfactual is vague. We are concerned with exposure. We observe what happens with exposure; a counterfactual is what we observe happens when there is no exposure, all else being equal.
- 1-15, line 15. While this is true, clinical studies also have the potential of overestimating effects when exposures used (concentration or intensity) are seldom experienced in the real world.
- 1-16, line 15. "discongruities?" – the meaning is opaque here.
- 1-18, line 16. It's not clear how analogy would not apply to the gaseous pollutants.
- 1-20, line 5. Coherence also refers to comparison of effects across study designs and across study endpoints.
- 1-20, line 27. I would argue that not meeting the temporality criterion, when it can be assessed, rules out causality.
- 1-23, line 1. I don't know what the authors are getting at here in comparing incidence and severity.
- 1-25, line 3. This discussion is unclear. If the point is that estimated mean population effects do not reflect more extreme effects in individuals that would be more clinically relevant, then please say that. If that is not the point, start again.

#### **Chapter 5. Modes of action.**

Figure 5.5. The emphasis here is on initial pulmonary oxidative stress and inflammation which “spills over” systemically. There should now also be an arrow going directly from autonomic modulation to systemic oxidative stress and inflammation, based on the Gonzalez-Flecha work.

## **Chapter 6. Acute health effects.**

### 1. Selective highlighting of positive results (a perennial issue); see Ch.1 comments (point 3.iii).

In the review of individual study findings, as in previous CDs, there continues to be an obvious tendency to report the positive findings, even though these might be one of among several endpoints. For example, in the review of controlled human exposure studies on HRV, findings from some generally negative studies (Peretz, Gong [6-18, line 23), etc) are summarized by highlighting the one or two positive findings selected from a host of the many possible findings from among the many time windows in which HRV was measured and the many HRV measures that were analyzed.

One flagrant example of this tendency is the summary of the Diez-Roux MESA study of CRP (6-52, line 28) which found no PM effects for lags up to one week. When the averaging period was extended up to 30 or 60 days, a small effect on increased CRP was observed. Effects observed over those long averaging periods are probably uninterpretable, however. This is reported as a “positive” study in the ISA. This finding is highlighted in the section summary (6-103, line 8). Here the result was characterized as being “stronger” at these long averaging times, when in fact it was only present at these averaging times.

Having said that, compared to earlier CDs, a better job is done in the ISA of summarizing effects on a comprehensive array of endpoints, regardless of whether these were highlighted by the original authors.

2. In reviewing the toxicological findings, it might be better to distinguish instillation studies from inhalation studies.

3. The assessments of causal determination (section 6.2.11; pp. 6.98-109) are not particularly transparent. For example, what specifically is the rationale for claiming a causal relationship for PM<sub>2.5</sub>, but only that such a relationship is likely for PM<sub>10</sub>? And, why is PM<sub>10-2.5</sub> merely insufficient?

### Specific.

6-2, line 12. Differences in exposure measurement error may also contribute to between-city heterogeneity.

6-3, line 34. Transfer of effects is only a minor aspect of the measurement error issue in the 2004 CD, but is the only one touched on here in this overview.

6-8, line 1. Might add how the ApoE<sup>-/-</sup> mouse model of atherosclerosis differs from natural human atherosclerosis, eg, no coronary atherosclerosis, etc.

6-8, line 19. There is no reference to the Rowan paper.

Section 6-2.

I would consider including discussion of cardiovascular mortality here, even though Section 6.5 summarizes mortality in general.

6-38, line 1. Need to include in this summary the BAD vs. FMD finding.

6-55, line 24. Why is discussion on a study of oxygen saturation included in the section on systemic inflammation?

6-58, line 14, What is described here is not really hematopoiesis, simply changes in peripheral blood cell counts.

6-59, line 18. I would say the evidence here is limited and certainly inconsistent.

6-61, line 20. Although even for vWF, some epi studies showed increases while others showed decreases. Also, only the Liao 2005 study is referred to, not the 2004b or 2007).

6-83, table 6-2. The PM<sub>2.5</sub> MI Zanobetti and Schwartz reference should be 2006, not 2005.

6-88, line 13. How “more successful?”

6-106, line 3. It seems that the Mills (2008) study of DE that was almost entirely UFP should be included as a human clinical study here.

6-109. I suggest that a section on PM chemical components (i.e., 6.2.11.5) be included here in addition to just sections on the PM size fractions, although that is presented late in the chapter.

6-110, Table 6-5. I would not include the 1999 and 1998 studies of Boezen and Forsberg in this table. This table is for more recent studies.

6-112, line 4. Should be Table 6.7, not 6.6.

6-215, line 19. PM<sub>10</sub> findings were not robust to NO<sub>2</sub> in the Canadian multi-city study (6-206, line 27).

6-225, line 26. Regarding Villeneuve 2003, this is not a cohort. Line 29 indicates a 5.4% increase in CV mortality for same day lag, but Fig 6-24 instead shows the lag 1 effect. Also, as opposed to what is stated, the PM<sub>2.5</sub> effect is not quite significant (see Table 4 of the Villeneuve 2003 paper). For Fig 6-23 regarding PM<sub>2.5</sub>, for total mortality at same day lag, the effect should be negative (Table 3 of Villeneuve 2003), for CV mortality for lag 1 the effect should be at least as negative as -1.0%, and for respiratory mortality for lag 1 the graphed effect looks close to 3%, but this is not correct either. I would recommend checking the math that converts to the 10 $\mu$ g/m<sup>3</sup> increment and ensure that the graphed effects are correct.

6-251 (section 6.6.2.4). Several of the toxicological endpoints described here are associated with long-term exposure and belong in Ch.7 only.

## **Chapter 7. Chronic health effects.**

1. This chapter presents a reasonably balanced presentation of findings, with exceptions. The cardiovascular and birth outcomes sections are particularly good in this regard.

2. Regarding birth outcomes, specifically, one point that I did not see a discussion of was the potential for confounding by season. Air pollution and birth outcomes vary by season. Matching on time of the year of birth, for example, does not adequately address this. In both cohort studies and studies that use birth certificate data, the proper controls for preterm births, for

example, are not births occurring at the same time of the year as cases, but rather gestations of approximately the same duration. The influence of this potential source of confounding needs to be considered for the relevant studies.

3. The Respiratory Effects section (7.3) is an exception to the generally excellent nature of this chapter. There is a tendency to report primarily positive endpoints from studies with multiple endpoints, as well as a tendency to report as positive findings that are unquestionably negative; e.g., p.7-28, line 33 on asthma in the Kim 2004 study. The Pulmonary Function (7.3.2) section, especially, is poorly written and presents extraneous information (e.g., Oftedal study description p.7-33). Unjustified claims are made; e.g., about lack of reversibility and about the meaning of different lung function measures (p.7-34, lines 18-21). There is too much relaying of individual authors' interpretation of their own findings. Unjustified summaries are made; e.g., Pulmonary Inflammation (p.7-50), especially regarding woodsmoke effects (line 22). The overall conclusions regarding causality in this respiratory section, however, are reasonable.

4. My preference would be to include discussion of cohort studies that include cancer mortality endpoints (eg, Pope 2002) in the section that is currently limited to cancer incidence (section 7.5), rather than placing that discussion in the following section on mortality.

5. Regarding mortality, an example of how further analyses modify initially-reported dramatic findings is provided by the Beelen 2008 study of traffic-associated mortality in the Netherlands. Effects were dramatically lower than those estimated based on an earlier portion of the cohort (Hoek 2002). The Beelen study suggests that traffic-associated effects may not be greater than those due to PM itself, a finding at odds with that in the initial report. This perspective is not provided here, but is appropriate in a discussion of source- and component-specific effects. On another issue relating to mortality, section 7.6.7 on exposure time windows does not include the Krewski et al assessments on this question using the ACS cohort.

6. I would dispute that an expert elicitation provides much if any additional evidence or support (7-115, line 18).

#### Specific.

7-4, line 11. It is not appropriate to report estimated increases in CAC here in the Diez-Roux study as if these were meaningful, in light of the wide CIs that essentially center on 0, or no effect. At the least, these should be reported as null findings.

7-16. It is not clear why Table 7-1 shows only some selected endpoints, eg, for Puett et al.

7-21, line 9. "Modification" does not belong here.

7-32, Fig. 7-4. MMEF is synonymous with FEF25-75.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

3-30-09 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Particulate Matter Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.