UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

November 24, 2009

EPA-CASAC-10-001

The Honorable Lisa P. Jackson
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Subject: Review of *Integrated Science Assessment for Particulate Matter (Second External Review Draft, July 2009)*

Dear Administrator Jackson:

The Clean Air Scientific Advisory Committee (CASAC) Particulate Matter (PM) National Ambient Air Quality Standards (NAAQS) Review Panel met on October 5 - 6, 2009 to review the *Integrated Science Assessment for Particulate Matter (ISA), (Second External Review Draft, July 2009)*. The Panel also held a public teleconference on November 12, 2009 to discuss and finalize its draft report. In this letter, CASAC offers general comments on the ISA, followed by CASAC's consensus responses to the Agency's charge questions. Comments from individual panelists are also attached.

CASAC commends EPA's National Center for Environmental Assessment for its comprehensive effort to address the concerns and comments offered by CASAC in its review of the first draft ISA. EPA has improved the document and focused its presentation of a substantial body of evidence so that it now more clearly highlights the findings that are relevant to the Risk Assessment (RA) and the Policy Assessment (PA). As mentioned in its comments on the charge questions, CASAC also commends EPA for the continued evolution of the process for evidence evaluation. The five-level classification of strength of evidence for causal inference has been systematically applied; this approach has provided transparency and a clear statement of the level of confidence with regard to causation, and we recommend its continued use in future ISAs. The implementation of the Health & Environmental Research Online (HERO) database greatly enhances the ISA and facilitates its evaluation by providing electronic hotlinks to citations and study data. We support its further evolution to include abstracted, key findings.

With regard to the approach taken in the ISA, we find EPA's decision to focus the discussion of causality on $PM_{2.5}$ and $PM_{10-2.5}$ independently to be appropriate and supported by the scientific evidence. As stated in our earlier review of the 1st draft ISA, the handling of PM_{10} as a separate pollutant was problematic because it is comprised of the fine ($PM_{2.5}$) and the coarse ($PM_{10-2.5}$) fractions. CASAC also supports EPA's changes to the causal determinations for long-term exposure to $PM_{2.5}$ and cardiovascular effects (from "likely causal" to "causal"), for cancer and $PM_{2.5}$ (from "inadequate" to "suggestive") and for cardiovascular and respiratory effects of short-term exposure to ultrafine particulate matter (UFP) (from "inadequate" to "suggestive"). CASAC concurs with EPA's definition of "susceptible subpopulations" as those that have a greater likelihood of experiencing health effects related to PM exposure; and we find that the ISA offers a careful characterization of the factors that may contribute to increased susceptibility to PM-induced health effects.

In terms of welfare effects, the visibility valuation and preference studies help to demonstrate that there are levels of visual air quality which are consistently judged to be "unacceptable" at levels well below the current PM NAAQS in a number of different study areas, an important finding that is appropriately highlighted. CASAC concurs that Chapter 9 has been improved by the additional discussion of optical measurement methods. Added material provides further support for the proposed use of a new "PM light extinction" indicator, which would be both readily measurable and reflective of the human perception of visibility effects caused by PM pollutants. CASAC also concurs that the added discussions on climate forcing effects and on ecological effects of PM strengthen the chapter's coverage of these topics. Ultimately, EPA should move toward developing exposure-response relationships for ecological endpoints, perhaps in the next review cycle for PM.

We have two major suggestions for improvement:

- The ISA could be strengthened by providing more information on the correlations of concentrations of PM_{10} with those of $PM_{2.5}$ and $PM_{10-2.5}$, preferably stratified by region of the country, in order to better understand PM_{10} as an indicator of the two subfractions, $PM_{2.5}$ and $PM_{10-2.5}$. As currently written, the ISA uses PM_{10} findings to support $PM_{2.5}$ effects whereas the relevance of PM_{10} findings for $PM_{10-2.5}$ effects is left ambiguous. Because of the role played by the current PM_{10} standard, PM_{10} findings that are particularly relevant to $PM_{10-2.5}$ should also be highlighted.

- CASAC recommends "upgrading" the causal classification for $PM_{2.5}$ and total mortality to "causal" for both the short-term and long-term time frames. There are epidemiological studies showing a positive association of all-cause mortality with $PM_{2.5}$. We acknowledge that the association is weaker for all-cause mortality (in comparison with cardiovascular mortality), but cardiovascular deaths are the largest component of total

deaths attributable to PM. If $PM_{2.5}$ effects for cardiovascular mortality are "causal," they must also be "causal" for total mortality, and the weaker association with all-cause mortality would be anticipated.

CASAC recommends that future assessments more fully consider evidence on the compositional differences in PM effects in relation to both health and welfare, especially given the emerging view that metals and carbonaceous aerosols, typically referred to as elemental and organic carbon, are of greater concern for many endpoints.

CASAC agrees that the PM ISA will be adequate for rulemaking after EPA incorporates our major comments and recommendations as stated above. We thank the Agency for the opportunity to provide advice on the PM ISA.

Sincerely,

/Signed/

Dr. Jonathan M. Samet, Chair
Clean Air Scientific Advisory Committee

Enclosures:
A. CASAC Particulate Matter Review Panel Roster
B. CASAC Responses to Charge Questions
C. Individual Responses to Charge Questions

Enclosure A

Clean Air Scientific Advisory Committee
Particulate Matter Review Panel

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Dr. James Crapo, Professor of Medicine, Department of Medicine, National Jewish Medical and Research Center, Denver, CO

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* / Unable to participate in this review.

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Dr. Joseph Helble, Dean and Professor, Thayer School of Engineering, Dartmouth College, Hanover, NH

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Enclosure B

Integrated Science Assessment for Particulate Matter
(Second External Review Draft, July 2009)

CASAC Responses to Agency Charge Questions

1) Evaluation of the health evidence in Chapters 6 and 7:

a) In response to the CASAC PM Panel comments about the determinations of causality for PM_{10}, we have refocused the evaluation of health effects resulting from exposure to PM_{10}. PM_{10} studies are now included where they provide insights into general relationships between PM and its effects, such as concentration-response relationships. Separate causality determinations are no longer presented for PM_{10}; however, PM_{10} study results are considered in causality determinations for $PM_{2.5}$ and $PM_{10-2.5}$ where appropriate. Please comment on this approach to evaluation of evidence from studies of PM_{10}.

At the April 2009 review of the first PM ISA draft, CASAC noted that findings on PM_{10}, $PM_{2.5}$ and $PM_{10-2.5}$ were often discussed as if these were separate pollutants, even though the $PM_{2.5}$ and $PM_{10-2.5}$ fractions comprise PM_{10}. This led to inconsistencies in causal determinations, since these were provided for each of the three PM indicators independently. In this draft, causal determinations are no longer provided for PM_{10} as they were in the initial draft of the ISA.

Motivation for dealing with PM_{10} as a separate entity, at least in the setting of short-term exposure, came from the continuation of the 24-hour PM_{10} standard. Given the different sources and the differing chemical compositions of the $PM_{2.5}$ and $PM_{10-2.5}$ fractions of PM_{10}, and to some extent the evidence for differing toxicity, there is little scientific justification for dealing with PM_{10} as a single entity. The approach taken in the current draft is therefore more in keeping with the state of the science.

Findings pertaining to PM_{10} in this 2nd draft are discussed alongside those of the two component fractions. There was obviously (and understandably) a need to consider the extensive findings pertaining to PM_{10} when evaluating the evidence on $PM_{2.5}$ and $PM_{10-2.5}$ since both fractions comprise PM_{10}. Findings on PM_{10} should have some relevance to evaluating evidence on $PM_{2.5}$ and $PM_{10-2.5}$. However, the relevance of evidence on PM_{10} to $PM_{2.5}$ or to $PM_{10-2.5}$ likely varies across the country. For example, in some regions of the country PM_{10} is more reflective of $PM_{2.5}$ whereas elsewhere PM_{10} is more reflective of $PM_{10-2.5}$. The charge question states that "PM_{10} studies are now included where they provide insights into general relationships between PM and its effects, such as concentration-response relationships. PM_{10} study results are considered in causality determinations for $PM_{2.5}$ and $PM_{10-2.5}$ where appropriate." For example, Figure 6-6 (p.6-120) shows a typical concentration-response relationship for short-term PM_{10} exposures and is offered as providing insight into the "PM" concentration response relationship. "PM" is a general designation and used without sufficient specificity in this context.

PM_{10} findings are also used in evaluation of the long-term effects of exposure to specific PM fractions (e.g., p. 7-24). For effects of long-term PM exposure on respiratory morbidity, the specific finding is made that "studies showing associations only with PM_{10} were conducted in locations where PM was predominantly fine particles, providing support for associations with long-term exposure to fine particles" (p. 7-28, line 32; p. 7-60, line 16). PM_{10} findings are used in support of findings on $PM_{2.5}$. However, in some of the referenced studies, associations were found for PM_{10} only and not for $PM_{2.5}$ (p. 7-43, line 6), a finding not consistent with the cited statement.

In the respective PM fraction Summary and Causal Determinations sections, there is little mention of PM_{10}. However, when findings on PM_{10} are mentioned in this context, they are only offered in regard to $PM_{2.5}$ (e.g., PM_{10} findings are cited as strengthening the evidence for $PM_{2.5}$-related respiratory effects [p. 6-244] and for mortality effects [p. 6-317]). PM_{10} evidence is not used in support of $PM_{10\text{-}2.5}$ effects. Yet in the discussion of short-term PM exposure mortality effects (section 6.5.2), PM_{10} studies are cited as providing "an underlying basis for the overall pattern of associations observed when examining the relationship between $PM_{10\text{-}2.5}$ and $PM_{2.5}$ and mortality." We urge more consistent handling of the PM_{10} evidence.

In order to better interpreting PM_{10} findings relative to those of $PM_{2.5}$ and $PM_{10\text{-}2.5}$, it would be helpful, perhaps in Chapter 3, to include and/or highlight data on the relationships of PM_{10} with both $PM_{2.5}$ and $PM_{10\text{-}2.5}$, stratified by region of the country. Also, in consideration of the role of the current 24-hour PM_{10} standard with respect to $PM_{10\text{-}2.5}$, it would be important to better document the relevant evidence on the relationship between PM_{10} and $PM_{10\text{-}2.5}$ across the country.

In summary, the extensive evidence on PM_{10} is used without specificity or consistency. PM_{10} evidence is used to support the occurrence of overall effects of PM, but specifically in support of effects of $PM_{2.5}$ but not of $PM_{10\text{-}2.5}$. The current PM_{10} standard, however, is in place for control of $PM_{10\text{-}2.5}$. Nevertheless, providing causality judgments for $PM_{10\text{-}2.5}$ and $PM_{2.5}$, but not for PM_{10}, as in the current draft, is more in line with the current scientific understanding.

b) **In the first draft ISA, causal judgments were made for cardiovascular morbidity, respiratory morbidity, and all-cause mortality. In the second draft PM ISA, causal judgments were made for cardiovascular effects, and respiratory effects, using evidence from both morbidity and mortality. New sections were included within cardiovascular and respiratory effects for cause-specific mortality in Chapters 6 (Sections 6.2.11 and 6.3.9, respectively) and 7 (Sections 7.2.10 and 7.3.8, respectively) that draw upon the more complete discussions of this evidence in the later mortality sections (Sections 6.5 and 7.6). These latter sections continue to present evidence of cause-specific mortality, as it informs the discussions and causality determinations for all-cause mortality. Furthermore, important results of analyses that examined potential effect modifiers, potential confounding by copollutants, PM-mortality concentration-response relationships, and the influence of different modeling approaches on the PM-mortality relationship remain in Chapter 6, Section 6.5. Considering both mortality and morbidity as part of a suite of effects, in addition to the other considerations underlying causality judgments,**

In general, CASAC agrees with EPA staff's decision to link the determination of causal judgment to cause-specific cardiovascular and respiratory mortality. In addition, CASAC concurs with including cause-specific mortality within the outcomes considered in assessing cardiovascular and respiratory effects. New evidence, primarily epidemiological in nature, published since the last review cycle, makes such a judgment possible and informative. Because much of all-cause mortality is comprised of cardiovascular and respiratory deaths, it is appropriate to show these two groupings separately. By showing these two classes of death separately, the reader can better appreciate both the magnitude and nature of the deaths attributable to $PM_{2.5}$.

CASAC finds that the available scientific evidence supports the judgment of a "causal" determination for short-term and long-term effects of $PM_{2.5}$ on cardiovascular effects. CASAC also supports the determination of a causal association between short-term and long-term effects of $PM_{2.5}$ exposure and total mortality, based both on the relevant scientific evidence and the finding of a causal association for cardiovascular mortality, which makes up a substantial proportion of total mortality. Yet, despite strong associations with these cause-specific effects, total mortality is less strongly and more variably associated with $PM_{2.5}$, perhaps because total mortality includes a number of categories more weakly linked to $PM_{2.5}$ or not all associated with $PM_{2.5}$. Consequently, long-term exposure to $PM_{2.5}$ was judged "likely to be causal" for total mortality. This determination might be justified when considered in the context of the epidemiological data on all-cause mortality alone, but it is not consistent with the classification of cardiovascular mortality as "causal," given the substantial contribution of cardiovascular mortality to all-cause mortality. Specifically, on page 2-18 the ISA states that "a causal" relationship exists between long-term exposures to $PM_{2.5}$ and cardiovascular effects, yet on 7-137 the ISA states that "the relationship between long-term $PM_{2.5}$ exposure and mortality is likely to be causal." Because the impact of PM on cardiovascular effects is judged "causal," and since cardiovascular mortality is the largest contributor to total mortality, CASAC believes that the association with total mortality should logically be classified as "causal" rather than "likely causal." While cardiovascular mortality is the single greatest contributor to total mortality, other causes are less well associated with $PM_{2.5}$ and some conditions not at all. Because total mortality is strongly related to cardiovascular events, consideration should be given to explaining why the available studies addressing all-cause mortality appear to be conclusive, by carefully explaining the contribution of other less strongly associated conditions. CASAC concurs with the conclusion of a "likely to be causal" association between respiratory effects and long-term and short-term exposures to $PM_{2.5}$.

The added sections included in the ISA are effective in summarizing the recently reported evidence and in providing a basis for the causal determinations. As the ISA process matures and

continues to evolve, CASAC recommends that a table be included that lists the previous review cycle's causal judgment determinations directly beside the current cycle determinations, with a brief comment about what has changed in the informational database to warrant a change in the causal classification. This table would provide the reader with a valuable summary of the historical process, and document changes in knowledge and interpretation that form a critical part of NAAQS evaluation.

c) **We reexamined the controlled human exposure and toxicological studies of fresh diesel and gasoline exhaust and determined that while these exposure atmospheres contain relatively high mass concentrations of $PM_{2.5}$, the particle number count distribution was predominantly in the ultrafine size range. Therefore, for the second draft ISA, we considered the diesel and gasoline exhaust studies, in addition to the other considerations underlying causality judgments, when making our causal determinations for ultrafine PM exposure and cardiovascular and respiratory effects, resulting in a change from "inadequate" to "suggestive" for both categories. Diesel and gasoline exhaust studies also continued to be considered as part of the evidence for $PM_{2.5}$ health effects, as was done for the first draft ISA. With consideration of this rationale, please comment on the scope of evidence considered in the causal determinations for ultrafine PM.**

CASAC agreed with EPA's rationale in moving the causal determination for UFP from "inadequate" to "suggestive". Much of the evidence provided from clinical exposures and toxicological studies is based on gasoline or diesel exhaust studies, and combustion of these fuels generates high levels of -UFP. Epidemiological investigations have been less specific in their assignment of health outcomes specifically to UFP, although an increasing number of studies are observing effects of exposures proximal to roadsides, reflecting some component of combustion exhaust or vehicle operation. While additional research is needed, we concur with changing the causal determination for UFP from "inadequate" to "suggestive."

d) **The CASAC PM Panel recommended that we further consider the evidence related to PM exposure and cancer. Section 7.5 (Cancer) was revised to include evaluation of epidemiologic studies of both mortality and incidence of cancer with exposure to PM, as well as a brief overview of the toxicological evidence conducted using intratracheal instillation or dermal routes of exposure to better characterize the role of PM in mutagenicity, genotoxicity, and carcinogenicity. As a result of revisions to this section, the causal determination for $PM_{2.5}$ and cancer was changed from "inadequate" to "suggestive"; the causal determination for $PM_{10-2.5}$ remained unchanged. Please comment on the expansion of this evaluation to include a summary of toxicological studies using routes of exposure other than inhalation, as well as consideration of both mortality and incidence studies.**

EPA has carefully summarized a complex literature related to both the general and specific findings of mutagenicity, genotoxicity and carcinogenicity studies on PM and cancer. The charge question has two components. First, publications in toxicological studies to assess mutagenicity and genotoxicity on mechanisms for mammalian cancer research have used routes of exposure other than inhalation. For some agents, such studies have provided insights on potential cancer risks in humans. Thus, such data can be appropriately used for determining the degree of certainty with regard to causality. Second, with regard to the recently reported findings of epidemiological studies, these have included large, well assessed populations and they have shown associations with cardiovascular and respiratory outcomes. The same approach has been used for lung cancer, although interpretation is complicated by the possibility of potential confounding by smoking. With the exception of one relatively large European study that was null, these studies show an association of PM exposure with cancer risk that is robust after controlling for smoking. These studies provide support for the "suggestive" classification, particularly in the context of other lines of evidence reviewed in the ISA.

2) **Revisions to Chapters 1 (Introduction), 4 (Dosimetry), and 5 (Mode of Action): Changes to these chapters included expansion or clarification in a number of areas, as presented in more detail in the recent letter from EPA's Administrator. These included expansion or addition of sections on the history of the previous PM NAAQS review in Chapter 1; deposition and clearance of particles in Chapter 4; and epigenetics, lung development, atherosclerosis and consideration of acute and chronic responses in Chapter 5. Please comment on the revisions to these chapters.**

We commend the organizers and authors of this document for providing the CASAC PM Panel with well organized and readily readable texts for Chapters 1, 4, and 5 that are, for the most part, thorough and accurate in presenting the peer-reviewed literature most relevant to an Introduction (Ch. 1), Dosimetry (Ch. 2), and Mode of Action (Ch. 3). The amount of text on UFP could be condensed, especially in Chapter 5, where the potential to cause adverse effects is so prominently featured, along with the implication that particle number concentration is the most important metric for risk. Some additional discussion of still weak evidence in support of this hypothesis is warranted. There is inadequate discussion of the usefulness of the limited data on ambient air UFP concentrations currently available. The data are essentially limited to particle number concentrations, which make no distinction with respect to particle composition. The likelihood of effects is likely to differ among UFPs formed as condensation aerosols of sulfuric acid droplets, metal oxides, elemental carbon, and organic carbon, and with the changes in composition and particle size with residence time in the ambient air.

3) **Evaluation of susceptible population groups in Chapter 8: In response to the CASAC PM Panel comments, we have now focused specifically on susceptible subpopulations (defined for this ISA as those subpopulations that have a greater likelihood of experiencing health effects related to PM exposure) in Chapter 8. The introduction of this chapter was revised to include this new definition of susceptible subpopulations, recognizing that the terms susceptible and vulnerable have sometimes been used interchangeably in the literature, and in other cases have been used to represent two different categories (i.e., biological factors [e.g., age gender, etc.] vs. non-biological factors [e.g., SES, differential exposure, etc.]), resulting in the lack of a clear and consistent definition. The discussion was reorganized to improve the characterization of**

factors that may contribute to increased susceptibility to PM-induced health effects. Each section was also revised to include the different exposure durations (short- and long-term) and PM size fractions examined in the studies discussed within each subsection of the chapter. Please comment on the organization and presentation in Chapter 8 of evidence regarding susceptible subpopulations.

The organization and presentation of Chapter 8 is complete, clear and well-organized. The authors have been responsive to CASAC's critique of the first draft of the chapter. The definition of "susceptible" is clearly stated with a rather complete listing of how the term has been used in the literature in the past. We recommend that the authors consider identifying those definitions which are most timely and relevant for the purposes of this chapter.

Table 8-2 introduces all susceptibility factors that have been evaluated, as well as the particle size fraction evaluated and the duration/length of exposures. Table 8-2 is followed by a more detailed description of the evaluations that were made. This is a highly appropriate organization that could be improved by the addition of a column to the table which briefly summarizes the impact of each susceptibility factor on health impacts and/or observed health effects. The title of the table "Susceptibility Factors," gives the impression that all factors listed determine susceptibility, but some of those listed, such as gender, do not. Therefore, the title could be modified to "Susceptibility Factors That Have Been Evaluated" to more accurately reflect the contents of this table. The addition of a column to the table to indicate the results of each evaluation with a simple plus/minus summary approach would further improve the presentation.

4) **Revisions to Chapter 3 on Source to Exposure: Consistent with revisions made to the health effects chapters, Chapter 3 was revised to clarify that PM_{10} incorporates both $PM_{2.5}$ and $PM_{10-2.5}$ and reorganized to begin with $PM_{2.5}$ and $PM_{10-2.5}$, followed by PM_{10}, where applicable. The discussion of measurement techniques and chemistry of $PM_{10-2.5}$ has been expanded in Sections 3.4 and 3.5, in response to CASAC comments. In addition, Section 3.8 on human exposure to PM has been reorganized and expanded to better characterize the evidence and provide useful information for interpretation of epidemiologic studies. We would appreciate comments from the CASAC PM Panel on these revisions.**

The Chapter is a comprehensive summary of the current state of the evidence on PM sources, ambient aerosols, monitoring and modeling methods, concentrations and exposures. The Chapter generally reflects the state of science in a clear, comprehensive, and well organized fashion. Further, the Chapter revision appropriately incorporates comments from the April review. Of note, the relationships among $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} were clarified, although some additional information could be pulled forward from the Appendix (see below). The inclusion of additional information on UFP, PM components, and $PM_{10-2.5}$ monitoring methods was also an improvement. Similarly, the organization and content of the exposure section was greatly improved, and the relevance of exposure findings to interpretation of the results of epidemiologic studies was more fully addressed. While significantly improved, further improvements could be made to the exposure section to help with the organization, seeming overlap with earlier sections, and clarity, as discussed below.

Specific comments:

- The Chapter would benefit from a more detailed discussion of the relations among ambient PM_{10}, $PM_{2.5}$, and $PM_{10-2.5}$, particularly for the 15 cities selected for more detailed analysis. While this information is in the Appendix, it would be helpful to bring a summary of the findings into the main chapter.

- The distinction between primary and secondary organic aerosols should be expanded to discuss the potential for oxidation of primary organic particles which makes them become similar to secondary organic aerosol.

- Standard Reference Materials (page 2-20, line 20): It says "To date, there are few standard reference materials ..." This sentence should be reworded to make clear that we currently do not have a way to assess mass concentration measurement accuracy, as there are no standard reference materials (SRMs) or equivalent standards (to our knowledge) that provide a test of accuracy or airborne PM mass. There are, however, SRMs that are useful for testing the accuracy of the analytical methods for PM composition.

- Policy Relevant Background (PRB): The EPA promulgates a health-based standard irrespective of the background concentration of particles and thus, the PRB primarily has implications for implementation. If the PRB increases because of sources outside of the United States, there will be greater difficulty in attaining concentrations that are fully protective of public health. The modeling approach to establishing PRB has some appeal, but given the inaccuracy of emissions inventories in the US, where substantial effort and resources have been expended to develop them, there is little likelihood that we can adequately model emissions for the rest of the world. Consequently, the ISA might also offer comparisons between the model-based approach and the remote site approach to assess the certainty of the model-based estimation of the PRB.

- Exposure Section: Given the relevance of the measured PM concentrations in the earlier sections of the Chapter, and for interpreting the epidemiological studies and the Health RA, discussion of exposure measurements should be placed before that for exposure modeling. Further, the exposure measurements section should include discussion of new methods to measure (1) personal exposures to total PM, (2) PM of outdoor origin, (2) ambient concentrations outside individuals' homes, and (3) indoor PM exposures to total PM and to PM of outdoor origin). In this context, studies using tracers of outdoor or regional pollution can be introduced.

    - The discussion of each topic should be consolidated into single sections, with references to this section made as necessary in later sections. As currently written, certain topics, such as spatial variability and particle infiltration, appear repeatedly in several subsections. The discussion on these topics would be more focused and less confusing if consolidated.
    - In Section 3.8.4.3, it would be helpful to clarify which component of PM is discussed. Further, within each subtopic or heading, separate or otherwise distinct discussions for $PM_{2.5}$, $PM_{10-2.5}$ and the PM components would improve clarity.

- Section 3.8.4 (Exposure Assessment Studies at Different Spatial Scales) and its subheadings are misnamed. While the heading titles do provide parallels with earlier sections of Chapter 3, they do not accurately describe the contents. For example, section 3.8.4.1 does not actually discuss urban scale ambient PM exposure, but issues related to exposure error, exposure modeling, and tracers of ambient particles.
- It would be helpful to include a subsection in the beginning of the section, perhaps in Section 3.8.1 (General Exposure Concepts) that summarizes the range of measured exposures to $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10}, their composition, and differences by city, susceptible group, and season.
- Section 3.8.6: Other factors that could affect exposures should be noted, such as home ventilation `and activity patterns.

5) **Integrative Synthesis in Chapter 2: The CASAC PM Panel recommended expanding Chapter 2 to include all important findings of the PM ISA. The integration of health evidence in Chapter 2 was reorganized to focus on effects of $PM_{2.5}$, $PM_{10-2.5}$, and ultrafine particles, and was expanded to include discussions of effects for which a "suggestive" causality determination was drawn. New integration sections were added that combine the evidence for health effects of $PM_{2.5}$, $PM_{10-2.5}$, and ultrafine PM across exposure durations. In addition, these integration discussions incorporated evidence related to mode of action, dosimetry, atmospheric chemistry, and exposure assessment to the extent possible. When appropriate, figures were added that summarize the overall U.S. and Canadian epidemiologic evidence for specific size fractions and exposure durations, along with the concentrations reported in the studies or provided by study authors. A new section was also added to Chapter 2 that contains policy-relevant considerations, including summaries for the evidence for susceptible subpopulations, lag structure of associations in epidemiologic studies, and the PM concentration-response relationship. Please comment on these revisions and additions to the integration of health effects evidence in Chapter 2.**

Overall, CASAC commends EPA for an excellent draft of Chapter 2. The chapter appropriately addresses CASAC's previous comments from the April review of the 1st draft ISA. The revisions as described in the charge questions are appropriate and enhance the content and structure of the chapter.

Although the current draft of Chapter 2 is excellent, it could be strengthened with selected revisions. The main technical points that should be addressed in finalizing this chapter are: (a) more attention is needed to the role of variability in the composition of PM by size fraction with respect to both health and welfare effects; (b) more analysis and discussion of PM effects on climate is needed, particularly with regard to the role of PM composition and its implications for adverse or beneficial effects; (c) additional synthesis is needed to more clearly tie together material related to PM characteristics and impacts on both health and welfare, including strength of association, and the implications of uncertainties; (d) there should be more effort to move toward exposure-response relationships for ecological effects endpoints; and (e) the conclusion regarding only a "likely" causal relationship between long-term exposure to $PM_{2.5}$ and mortality

should be carefully revisited, since there is evidence that the relationship exists with more weight of evidence than conveyed in the document.

Section 2.3 should have one summary table of all health effects, and the discussion should start with those effects for which there is the strongest weight of evidence, moving to those with weaker or no weight of evidence (rather than vice versa as in the second draft ISA). Some portions of Chapter 2 may be too detailed, such as the text on pages 2-24. There are places throughout Chapter 2 (e.g., page 2-13) where citation of later sections of the report would help readers in finding more detail to support the summary statements. Although Figures 2.1, 2.2, and 2.3 are generally very useful, they would be easier to interpret if disaggregated into figure panels, each addressing only one outcome. Furthermore, there appears to be an error in the scale at the bottom of Figure 2.3. Although there is a lower correlation of PM_{10} with $PM_{2.5}$ (Page 2.5, lines 14-19), the correlation for PM_{10} is nonetheless remarkably high and should be interpreted more appropriately.

The discussion of PM and climate concludes with an ambiguous summary statement that "a causal relationship exists between PM and effects on climate." This use of the term "effects" is inconsistent with causality statements elsewhere in the ISA, where the PM effects being considered were consistently and unquestionably adverse. In the case of climate, PM can exert both positive and negative climate forcing influences. Some discussion should be offered to frame and further clarify this issue, perhaps in Chapter 1.

CASAC recommends that EPA add more material regarding PM composition, an overall synthesis of both health and welfare effects, and a synthesis of the most significant uncertainties and their implications for the robustness of conclusions.

6) **Welfare effects evaluation in Chapter 9: Several revisions were made to the evaluation of the welfare effects evidence in Chapter 9, in response to the CASAC PM Panel comment, to focus further on effects on climate and ecosystems and include further evaluation of urban visibility evidence, where possible. In addition, as recommended by the CASAC PM Panel, key findings and conclusions from this chapter were incorporated in Chapter 2. The discussion of PM effects on climate was increased with substantially more detail from recent publications, including discussion of specific climate forcing effects from individual PM components and size fractions. The discussion of ecological effects was also reorganized to focus on the types of effects and effects of individual components. For the effects of PM on visibility, new material was added including sections on direct optical measurements and the value of good visual air quality. Please comment on the effectiveness of the reorganization and revisions regarding welfare effects.**

CASAC was pleased to note the effective addition of sections on “Ecological and Welfare Effects” in the Integrative Overview summary discussion in Chapter 2. CASAC also agreed that the revisions to discussions of PM welfare effects in Chapter 9 strengthen the chapter, improve its clarity and are directly responsive to previous CASAC comments on the 1st Draft ISA. Several minor revisions would be helpful to improve accuracy in some sections (see individual panelist comments for detail), but no major revisions are needed.

Newly added details on climate, ecological and materials effects of PM and its various components provide more comprehensive coverage of these important subject areas; however, concentration-response functions for climate and ecological endpoints will be needed for future ISAs. Information in Chapter 9 on optical measurement methods provides added support for the proposed use of a new "PM light extinction" indicator, which is readily measurable and directly reflects the human perception of visibility effects caused by PM. The section on night-time visibility in Chapter 9 is important and should be brought forward to the summary chapter (Chapter 2). The information presented on visibility valuation and preference studies helps to demonstrate that visual air quality is consistently judged to be "unacceptable" at levels well below the current PM NAAQS in a number of different study areas. The findings in the ISA are sufficient to propose levels of PM light extinction above which public welfare is affected adversely. Finally, it is important to recognize, as the ISA does, the very substantial welfare effects from airborne PM, NO_x and SO_x are addressed in a separate NAAQS review.

Enclosure C

Compendium of Individual Comments

CASAC Particulate Matter Review Panel

Integrated Science Assessment for

Particulate Matter (Second External Review Draft, July 2009)

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Cascio Comments (Dr. Wayne Cascio) 8

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Ashbaugh Comments (Dr. Lowell Ashbaugh)

Charge Question 6:

Several revisions were made to the evaluation of the welfare effects evidence in Chapter 9, in response to the CASAC PM Panel comment, to focus further on effects on climate and ecosystems and include further evaluation of urban visibility evidence, where possible. In addition, as recommended by the CASAC PM Panel, key findings and conclusions from this chapter were incorporated in Chapter 2. The discussion of PM effects on climate was increased with substantially more detail from recent publications, including discussion of specific climate forcing effects from individual PM components and size fractions. The discussion of ecological effects was also reorganized to focus on the types of effects and effects of individual components. For the effects of PM on visibility, new material was added including sections on direct optical measurements and the value of good visual air quality. Please comment on the effectiveness of the reorganization and revisions regarding welfare effects.

The revisions are quite good; the authors have done an excellent job of incorporating comments from the earlier review. The integration of welfare effects into Chapter 2 works well. I would like to see a short paragraph in Chapter 2 summarizing the effects of PM on nighttime visibility. I especially liked the section on nighttime visibility in Chapter 9 on page 9-8. The paragraph on lines 22-30 of page 2-37 is not clearly written. Twice in succession it states that the use of a no-threshold log-linear model is supported, but then cites other studies that suggest otherwise. It would be good to revise this paragraph to more clearly state – well, I'm not sure what. Probably that more research is needed.

Chapter 9 is also much improved. The organization is good, and small details make it easier to read. For example, the spatial contour plots are much easier to compare now that the contour scales are similar for related figures. The haze trends figures (9-26 & 9-27) would benefit from using a color other than yellow, though, which does not show up clearly. Or perhaps the yellow (up) and light green (down) arrows could have a black border. Then they would also be distinguishable from the red and dark green when copied in B/W.

I like Section 9.3.1 but the figures would benefit from better reproduction. Most of the figures copied from the CCSP SAP2.3 did not reproduce well (also, the caption for Figure 9-70 contains a typo – "Arcic" instead of "Arctic"). Is it possible to obtain the originals?

The individual components discussion is well organized and easy to read. I'm familiar with one reference that could be added to the section on smelters and roadsides (page 9-245). The reference is "Resuspension of Soil as a Source of Airborne Lead near Industrial Facilities and Highways," by Thomas M. Young, Deo A. Heeraman, Gorkem Sirin, and Lowell L. Ashbaugh, *Environmental Science & Technology* **2002** *36* (11), 2484-2490. It seems to be relevant to the discussion. Here's the abstract:

> Abstract: Geologic materials are an important source of airborne particulate matter less than 10 μm aerodynamic diameter (PM_{10}), but the contribution of contaminated soil to concentrations of Pb and other trace elements in air has not been documented. To examine the potential significance of this mechanism, surface soil samples with a range of bulk soil Pb concentrations were obtained near five industrial facilities and along

roadsides and were resuspended in a specially designed laboratory chamber. The concentration of Pb and other trace elements was measured in the bulk soil, in soil size fractions, and in PM_{10} generated during resuspension of soils and fractions. Average yields of PM_{10} from dry soils ranged from 0.169 to 0.869 mg of PM_{10}/g of soil. Yields declined approximately linearly with increasing geometric mean particle size of the bulk soil. The resulting PM_{10} had average Pb concentrations as high as 2283 mg/kg for samples from a secondary Pb smelter. Pb was enriched in PM_{10} by 5.36-88.7 times as compared with uncontaminated California soils. Total production of PM_{10} bound Pb from the soil samples varied between 0.012 and 1.2 mg of Pb/kg of bulk soil. During a relatively large erosion event, a contaminated site might contribute approximately 300 ng/m(3) of PM_{10}-bound Pb to air. Contribution of soil from contaminated sites to airborne element balances thus deserves consideration when constructing receptor models for source apportionment or attempting to control airborne Pb emissions.

Avol Comments (Mr. Ed Avol)

1) Evaluation of Chapters 6 & 7 Health Evidence

(a) Evaluation of evidence from PM_{10} studies (lead discussant, Vedal)

The revised approach is well-presented and understandable. The authors and staff have done a commendable job in improving the accessibility of data, readability of the document, and documentation of the included information over the previous version.

I did not read the entire document (so I am not certain of this), but I did not readily see any discussion (or reference to a discussion) announcing, justifying, or explaining this decision to "collapse" PM_{10} into these other categories. For example, this might be justified on a scientific basis (high inter-correlation with coarse PM, for example) or possibly even a regulatory one (research evolving to smaller particle sizes). Did I miss this somewhere?

(b) inclusion of cause-specific mortality in the development of causal judgments (lead discussant, Cascio)

I agree with the decision to link the determination of causal judgment to cardiovascular and respiratory mortality, since these have been very active and productive areas of research since the last review cycle. The added sections are effective in summarizing the cumulative recent evidence and providing a basis for the causal determinations. As the ISA process mature and continue to evolve, it might be worth considering inclusion of a summary table that lists the previous review cycle's causal judgment determinations directly beside the current cycle determinations, with a brief comment about what has changed in the informational database to warrant a change in causal determination, This would provide the reader, the Staff, and the public with a readily trackable means of documenting changes in knowledge and interpretation that form a critical part of NAAQS evaluation.

Response to Charge Question 1c

(c) Scope of evidence considered in causal determination of UFP (lead discussant, Avol)

I agree with the rationale and thinking of the Staff and authors on moving the causal determination for UFP from "inadequate" to "suggestive". Although there is growing research activity in the effects of PM in this size range, there is still much that is not understood, appreciated, or being considered. This is complicated by the difficulty in generating and/or characterizing "reproducible" or "representative" UFP for study use at ambient exposure-appropriate concentrations. Additional concerns include observations that particle surface reactivity may be strongly related to fresh combustion and/or new particle formation, and observations that smaller particles seem to have increased toxicological properties.

(d) Inclusion of cancer mortality and incidence, additional routes of exposure (lead discussant, Speizer)

I agree with the expansion decision for both routes of exposure and consideration of both mortality and incidence studies.

2) Chapters 1 (Introduction),4 (Dosimetry),5 (Mode of Action) revisions

Comments on Chapter 1

(I repeat this comment from 1a, since it is relevant to the Chapter 1 Introduction)
I did not read the entire document (so I am not certain of this), but I did not readily see any discussion (or reference to a discussion) announcing, justifying, or explaining this decision to "collapse" PM_{10} into these other categories. For example, this might be justified on a scientific basis (high inter-correlation with coarse PM, for example) or possibly even a regulatory one (research evolving to smaller particle sizes). Did I miss this somewhere?

P. 1-2, first bullet – Three categories of exposures (short-term, chronic, and peak) are described in this carefully crafted opening list of review considerations…but short-term and chronic exposures are the focus of the documents. Should some comments, concern, consideration be focused on peak exposures, even if just to say we don't know much about it or need to learn more?

Comments on Chapter 4

P4-2, line 31 – Manufactured nanoparticles are not considered in this chapter (or in the review. Presumably manufactured nanoparticles lie somewhere on the continuum from completely unrealistic exposures to completely relevant ones…Are manufactured nanoparticles being considered as "occupational" exposures? Regardless, some thought should be given to the potential for population exposure to these particles, and what might be learnable from these engineered exposures (which may not be all that different from laboratory-generated exposures of TiO2 or other specifically generated artificial particles that serve an important purpose in identification of mechanisms and pathways). Would knowledge and consideration of their potential health effects (as a function of their particle size) be an appropriate section in an UFP chapter?

Comments on Chapter 5

I think this chapter was very well done and especially appreciated Section 5.6, which summarized new results AND provided references to the appropriate document section to read more detail about the individual finding.

The final text page of the chapter (5-31) "gaps in knowledge" is worthy of a section title or tabulation. In a larger document sense, this final summary and assessment of knowledge gaps would be useful additions to most every chapter in the ISA.

General Comments on PM ISA, 2nd Draft, Avol

In a large, data-rich, and complex document such as this, it would seem helpful to establish a consistent presentation paradigm that is followed throughout the relevant chapters, so that the reader can move from chapter to chapter, in or out of sequence, and still have some expectation of finding a consistent set of validators or signposts with which to review, interpret and integrate the presentations. Substantive progress has been made towards that objective in the ISA, but there still remain some inconsistencies that provide unnecessary obstacles to the reader. Here are two examples of this:

(1) A consistent PM-size-oriented summary presentation would help to establish a standardized format and framework for review. Accordingly, it would be useful if, in each Summary and Causal Determinations section of each chapter, health outcome, etc, a paragraph were denoted for $PM_{2.5}$, $PM_{10-2.5}$, and UFP and a brief summary statement regarding causality judgment -- for each size-cut – were made. (This comment motivated by the observation that UFP summary statements seem to be sporadically missing, such as in section 7.4.3).

(2) In Chapter 2 , there is (almost) a developed (and pragmatically useful) standardized listing of health outcomes, in five categories (cardiovascular; respiratory; mortality; reproductive and developmental; cancer, mutagenicity, and genotoxicity) that could be consistently evaluated against each of the pollutants under review for a current judgment of causal determination (from not likely to causal). These tabular summaries could then form the basis for guideposts to areas of needed future investigations, markers for progress from review to review, etc.
I suspect there is an error in the listed range of effects estimates in Figure 2-3 (P2-29); it is difficult to believe that the effects estimates range from -12 to +32.

7.2.11 Summary & Causal Determinations (of Cardiovascular and Systemic Effects)– Much improved and clearer, providing a basis for what was known prior to the current review, and what the new information shows. Summary judgments for $PM_{2.5}$, $PM_{10-2.5}$, and UFP all seem reasonable, but the supporting comment for UFP ("…due to a few studies being conducted without gaseous co-pollutants…" seems unnecessary and inaccurate, since the current breadth of studies reporting UFP and health associations is minimal, independent of adjustments for the presence or absence of gaseous co-pollutants. There may be some suggestions of effects and a valid concern for additional research, but at the time of this review, the cumulative import of observed effects in the assembled body of work is unclear and in need of additional investigation.

There still is appears to be an (unnecessary) tendency to discuss study after study after study at a level of detail that could be more appropriately placed in the annex. The main section of this document would be more useful as an integration of current knowledge, not an exhaustive listing of it; additional materials could and should be provided in the annex.

P7-27, lines 28-29 – "Evidence from these studies alone is inadequate to infer the presence or absence of a causal relationship due to a few studies being conducted without gaseous pollutants." This may be true, but can't the same comment be made for the studies reporting effects of PM_{10}, $PM_{2.5}$, and $PM_{10-2.5}$? Why make this point for UFP only?

Brain Comments (Dr. Joe Brain)

ISA-PM: Charge Question 5: Integrative Synthesis in Chapter 2

Overall, chapter 2 is much improved. Especially, making it a synthesis of the entire document makes sense. This is consistent with CASAC's recommendation regarding the first draft of the ISA. In particular, I like the delineation of the three critical size ranges of PM: coarse, fine, and UFP. These three size ranges are now prominent throughout and adequately discussed in terms of exposure and response. The inclusion of welfare considerations and ecological effects is well integrated into the chapter as a whole. *In toto*, this is an extremely valuable component of the ISA. It is a section which will be heavily used by policy makers, the scientific community, and the lay public. The authors are to be congratulated on producing a summary which is both sophisticated as well as accessible.

Section 2.4, "Policy Relevant Considerations," is done well. The role of susceptible populations is emphasized. This is important since these individuals make a dominant contribution to the observed health effects.

Cascio Comments (Dr. Wayne Cascio)

Charge Question 1a

General Comments:

1) The outstanding effort of the staff at NCEA to address the concerns and comments of the CASAC PM panel is very much appreciated, and has improved the document and focused the information in such a way as to more clearly justify the message it is designed to convey.
2) As discussed previously by the CASAC PM panel the determination of causality for PM_{10} is problematic as this fraction contains both the fine and coarse (thoracic PM) fraction, and its risk appears to be more strongly determined by the fine fraction. Consequently, the approach to focus the discussion of causality determination on $PM_{2.5}$ and $PM_{10\text{-}2.5}$ independently is appropriate, but appears to be at odds with the current PM_{10} standard. How does EPA intend to reconcile this discontinuity?
3) Nevertheless, the separation of PM into $PM_{2.5}$ and $PM_{10\text{-}2.5}$ is strongly supported by scientific data.
4) The concept that the abundant data on PM_{10} might serve to selectively support the causality determinations for $PM_{2.5}$ and $PM_{10\text{-}2.5}$ is problematic. As described above PM_{10} contains both fractions and there will always be uncertainty as to whether effects measured in response to PM_{10} are related to the $PM_{2.5}$ fraction, the $PM_{10\text{-}2.5}$ fraction or some combination of the two.

Charge Question 1c

General Comments:

1) The outstanding effort of the staff at NCEA to address the concerns and comments of the CASAC PM panel is very much appreciated, and has improved the document and focused the information in such a way as to more clearly justify the message it is designed to convey.
2) In Chapters 6 and 7 a comprehensive list of studies reporting health effects, toxicity of diesel emission and gasoline emission PM is provided. The rationale to include diesel and gasoline emissions as evidence of effects of UFP is reasonable given the strong association between PM mass from these source and particle number. Of relevance to this question are the results of our recently completed California Freeway Study that showed that particle number was most strongly associated with health effects endpoints in subjects exposed to traffic related pollutants on two Los Angeles freeways for 2 hours.
3) Based on the weight of the evidence with the inclusion of diesel and gasoline emission data the change in the causal determination for UFP from “inadequate” to “suggestive” is appropriate.
4) The presentation of diesel, gasoline and wood smoke emission data independently provides a means to quickly find relevant health effects data linking a specific exposure type to health effects. Such an approach was useful in judging the strength of associations and determination of causation.

Charge Question 1d

General Comments:

1) The outstanding effort of the staff at NCEA to address the concerns and comments of the CASAC PM panel is very much appreciated, and has improved the document and focused the information in such a way as to more clearly justify the message it is designed to convey.
2) In the 2nd external review draft Section 7.5 provides a more detailed presentation of epidemiological and toxicological data. The information is well integrated. This has improved the quality of information regarding the association between PM exposure and cancer.
3) In the first ISA the presentation of the possible link between PM exposure and cancer was judged as "inadequate". Now with better integration of epidemiological and toxicological data the causal determination has been changed to "suggestive". This change is appropriate based on the presented data. While toxicological studies included in this section were conducted with exposure routes other than inhalation these studies are important for providing a mechanistic basis to justify the biological plausibility of a causal determination.

Chapter 6

Specific Comments:

SEC/PAGE	PARA/LINE	REVIEW COMMENTS
6.2.1/2	1. 1 - 5	One can add that decreased HRV may precede some clinically important arrhythmias such as atrial fibrillation, and SCD in high risk populations. (Chen PS, Tan AY. Autonomic nerve activity and atrial fibrillation. Heart Rhythm 4(3 Suppl):S61-4, 2007; Thong T, Raitt MH. Predicting imminent episodes of ventricular tachyarrhythmias using heart rate. Pacing Clin Electrophysiol 30:874-84, 2007; Sandercok GR, Brodie DA. The role of heart rate variability in prognosis for different modes of death in chronic heart failure. Pacing Clin Electrophysiol 29:892-904, 2006)
6.2.1/2	2. 5-7	The sentence, "SDDN generally reflects…" can be rewritten, "SDDN generally reflects the overall modulation of HR by the autonomic nervous system, whereas rMSSD and frequency variations in HR

		generally reflect parasympathetic activity”.
6.2.1/2	2. 7-9	The sentence, “LF is predominately...” can be rewritten as “LF is predominately determined by both sympathetic and parasympathetic tone and increased LF/HF indicates sympathoexcitation,…”
6.2.1/6	1. 5-6	In the study by Yeatts et al. (2007, 091266) it is true that rMSSD but this was not statistically significant. P=0.16. Likewise, pNN50 did increase in response to PM2.5-10 but this result also did not reach statistical significance. P=0.07.
6.2.1/6	2. 7-9	In the study by Langrish et al. (2009, 191908). Did the authors confirm that the facemask did not affect the rate or depth of breathing. If not then it is possible that the results could have been influenced by the facemask.
6.2.1.2/13	2, 2	Space between “of” and “20”
6.2.2.1/21	1, 5-7	The sentence, “VPBs are …” should be rewritten. Consider the following, “VPBs are spontaneous beats originating from either the right or left ventricles. VT refers to 3 or more ventricular beats in succession at a rate of 100 beats per minute or greater, while VF is characterized by rapid and disorganized ventricular electrical activation incapable of generating an organized mechanical contraction or cardiac output.
6-22	1, 10 and 2, 1	The sentence, “Pathophysiologic mechanisms…” should be rewritten. Consider the following, “Pathophysiologic mechanisms underlying this established cause of sudden cardiac death include activators and facilitators of arrhythmia such as electrolyte abnormalities, modulation of the autonomic nervous system, membrane channels, gap junctions, oxidant stress, myocardial stretch and ischemia acting on myocardium conditioned for arrhythmia by altered by cellular and tissue architecture, fibrosis, and intracellular calcium handling.”

6-27	1, 7	The sentence, “Such beats…” should include the conduction system as a source of arrhythmia. For example, “Such beats can arise in the atria, AV node, conduction system, or the ventricles.
6-27	2, 1	“nonsmoking” to “non-smoking”
6-29	2, section heading	Change “ECG abnormalities indicating arrhythmia” to “ECG changes associate the modulation of repolarization”.
6-29	1, 4	A final statement might include, “Alternatively, novel non-invasive electrocardiographic telemetry systems might be used more effectively to assess the relationship between air pollutants and arrhythmia in patients with history of arrhythmias or at risk for serious arrhythmia.”
6-34	1, section heading	Change “ECG abnormalities indicating ischemia” to “ECG changes suggestive of increased ischemia”.
6-39	1, 1	Write out “yr” as “year”
6-39		Write “IHD” as “ischemic heart disease”
6-40	1, 1	Consider changing the first sentence to “…examine the association between 2 measures of vascular reactivity, non-endothelium dependent nitroglycerin mediated reactivity and endothelium-dependent flow-mediated reactivity, and ambient…”
6-48	1, 1	Write “ET” as “endothelin-1”
6-62	1, 4	“QA interval” should be defined.
Table 6-4/65		The closed bracket after m3 is supra-scripted and should not be.
6-69	3, 1-5	Continue “on markers of inflammation...” directly on the previous line without indentation.
6-75	2, 5	Substitute “highway police” for “troopers”
6-77	2, 1	Write “wood smoke” instead of “WS”

6-81	1, 2	Write “thrombin anti-thrombin complex” instead of “TAT”
6.2.10.5	2, 7	“associate” should be written “associated”
6-116	2	Consider “Co-pollutant” rather than “Copollutant”.
6-123	1, 17; 2, 7	Consider “multi-city” rather than “multicity”.
6-128	2, last line	Add to the final sentence such that it would read, “ Furthermore, the HRV result…including age and pre-exiting conditions and genetic polymorphisms modulating responses to oxidative stress.”
6-138	1, last line	Consider “co-pollutant” rather than “copollutant”. “Copollutant” is used throughout the document. If such a change is accepted then other examples should be found.
6-241	1,	Consider changing “nonasthmatics” to “non-asthmatics”.
References		
6-336		Aekplakorn – add Journal title
		Analitis – add Journal title
		Andersen – add Journal title
		Andersen – add Journal title and volume
6-337		Atiga – add Journal title
		Atkinson - – add Journal title, volume and pages
6-338		Bastain – add Journal title
		Bell – add Journal title

		Berger – add Journal title
		Brauner – add Journal title
6-339		Brook – add Journal title
		Burnett – add Journal title, volume and pages
		Caligiuri – add reference. “Presented at” ?
		Carlsten – add Journal title
6-340		Checkoway – add Journal title, volume and pages
		Chevalier – add Journal title
6-341		Chuang – add Journal title
		Ciencewicki – add Journal title
		D’Ippoliti – add Journal title
		Daniels – add Journal title, volume and pages
		Danielsen – add Journal title
		De Bruin – add Journal title
		De Haar – add Journal title
6-342		Dockery – add Journal title, volume and pages
		Dominici – add Journal title, volume and pages
6-343		Dusek – add Journal title
		Fairley – add Journal title, vol. and pages
		Fakhri – get reference
		Farraj – add Journal title
6-344		Franklin - – add Journal title, vol. and pages
		Gent – add volume
		Gerlofs-Nijland – add volume

		Gerlofs-Nijland - – add Journal title
		Gilmour – add Journal title
6-345		Godleski – add Journal title
		Gong – add Journal title, volume, and pages
6-346		Hanigan – add Journal title
		Happo – add Journal title
		Harkema – add Journal title, vol. and pages
		Harrod – add Journal title
		Hogervosrt – add Journal title
		Holguin – add Journal title
6-347		Host – add Journal volume and pages
		Inoue – add Journal volume
		Ito – add Journal title, vol. and pages
		Ito – add Journal title, vol. and pages
		Ito – add Journal title
		Jalaludin – add Journal title
		Janes – add Journal title
6-348		Johnson – add Journal title
		Katsouyanni – add Journal title, vol. and pages
		Klein-Patel – add Journal title
		Kleinman – add Journal title
		Kleinman – add Journal title
		Klemm – add Journal title, volume and pages
6-349		Laupacis – add Journal title

6-350		Le Tertre – add Journal title, vol. and pages
		Lee – add Journal title
		Levy – add Journal title
		Li – add Journal title
6-351		Lin – add Journal title
		Lippmann – add whole reference
		Lippmann – add whole reference
		Lisabeth – add Journal title
		Liu – add Journal title
		Ljungman – add Journal volume and pages
		Low – add Journal title
6-352		Mar – Epidemiol. Is redundant
		Mar – add Journal title
		Mar – add Journal title, vol. and pages
		Matsumoto – add Journal title
		McCreanor – add Journal title
		Metzger – add Journal title
6-353		Mills – add Journal title
		Murata – add Journal title
6-354		Mutlu – add Journal title
		Nadziejko – add Journal title, vol. and pages
		Nadziejko – add Journal title
		O'Connor – add Journal title
		O'Neill – add Journal title

6-355		Okin – add Journal title
		Ostro – add Journal title, vol. and pages
		Park – add Journal title
		Park – add Journal title
		Peel – add Journal title
		Pekkanen – add Journal title
		Peng – add Journal title
		Pennanen – add Journal title
6-356		Pereira – add Journal title
		Perez – add Journal title
		Peters – add Journal title
		Peters – add Journal title
		Peters – add Journal title
		Piedrahita – form of reference is not consistent with the others
		Pope – add Journal title
6-357		Prystowsky – add Journal title
6-358		Rodriguez – add Journal title, vol. and pages
		Rundell – add Journal title
		Samet – add Journal title, vol. and pages
		Samet – add Journal title, vol. and pages
6-359		Sarin – add Journal title
		Schwartz – add Journal title, vol. and pages
		Schwartz – add Journal title

		Schwartz – add Journal title
		Seagrave – add Journal title
6-360		Sheppard – add Journal title
		Sillanpaa – add Journal title
		Smith – add Journal title
		Steinvil – add Journal title
		Stolzel – add Journal title, vol. and pages
6-361		Sullivan – add Journal title
		Tamagawa – add Journal title
		Tankersley – add Journal title
		Thurston – add Journal title
6-362		Trenga – add Journal title
		Tsai – add Journal title
		Tunnicliffe – add Journal volume and pages
		Upadhyay – add Journal title
		Van der Werf – add Journal title
6-363		Vincent – add Journal title, vol. and pages
		Wellenius – add Journal title
		Wellenius – add Journal title
		Whitekus – add Journal title
6-364		Whitsel – add Journal volume and pages
		Wichmann – add Journal title, volume and pages
		Witten – add Journal title, vol. and pages
		Wong – add Journal title

		Yang – add Journal title
		Yue – add Journal title
6-365		Zabel – add Journal title
		Zanobetti – add Journal title
		Zanobetti – complete reference
		Zanobetti – complete reference
		Zanobetti – add Journal title, vol. and pages
		Zanobetti – add Journal title
		Zhang – add Journal title

Chapter 7

Specific Comments:

SEC/PAGE	PARA/LINE	REVIEW COMMENTS
7-2	L. 15-16	Consider "Atherosclerosis is a progressive disease that contributes to several adverse outcomes, including acute coronary syndromes such as myocardial infarction, sudden cardiac death, stroke and vascular aneurysms."
7-3	L. 31	Consider starting line 31 with, "CAC represents the accumulation of calcium in coronary artery macrophages and represents an advanced stage of atherosclerosis. As such CAC is a measure of…."
7-4	L. 3	Replace "AAC" with "Abdomenal aortic calcium (AAC)" at least initially when the term is introduced.
7-5	L. 3-4	Replace "anti-hyperlipidemic drugs" with "lipid lowering drugs".
7-5	L. 18	Replace "anti-hyperlipidemic drugs" with "lipid lowering drugs.

7-5	L. 24	Change font for "in 2002 (the midpoint of the baseline exam.).
7-11	L. 14	"decease" should be "decrease".
7-12	L. 14	Replace "TAT" with "Thrombin anti-thrombin complex (TAT)" at least initially when the term is introduced. For some of these terms that are use very infrequently throughout the text it is better to write them out and minimize the use of abbreviations.
7-14	L. 10	"non-statistically" does not meaningful. Consider "statistically non-significant".
7-14	L. 26	"nonsignificant" should be written as "non-significant".
7-14 and 15	L. 32-38 and L. 1-4.	There is no mention of renal function data in the Calderon-Garciduenas et al. 2007 paper. Yet, in the subsequent paragraph it is mentioned that no mention of an assessment of renal function.
7-19	L. 20	Replace "avg" with "average".
7-19	L. 22	Correct font of "respectively".
7-19	L. 27	Correct font of "$PM_{2.5}$".
7-20	L. 7	Replace "avg" with "average".
7-20	L. 9	Consider "The OR for fatal MI was increased but not significantly."
7-20	L. 13 and 26	Replace "avg" with "average".
7-21	L. 5	Replace "avg" with "average".
7-22	L. 17 and 22	Replace "avg" with "average".
7-22	L. 28	Write "hospital admissions" rather than "HAs".
7-59	L. 20	Change font of "reduction" and "reduced".
7-76	L. 16 and 17	Consider the following sequence, "Several age intervals have been explored: neonatal (<1 month), infants (<1 year), and post-neonatal (1 month to 1 year)." rather than what is present. Subsequently, on page 7-77 the

		order of presentation should follow this order.
7-77	L. 3-13	Move the paragraph "Infant Mortality and Infant Respiratory Mortality, <1 Year" after "Neonatal Mortality and Neonatal Respiratory Mortality, < 1 Month". "M" in "month" should be capitalized for consistency.
7-121	L. 14	Font of "reduction" and "reduced" should be corrected.
7-139		Achenbach – Title of journal
7-140		Arlt – Title of journal
		Baccarelli – Volume and pages
		Binkova – Title of journal
		Bobak – Title of journal
7-141		Brown – Title of journal
7-142		Craven – Title of journal
		Dales – Title of journal
		Dinneen – Title of journal
		Dockery – Title of journal
		Dugandzic – Title of journal
		Eftim – Title of journal
7-143		Fedulov – Title of journal
		Fujimoto – Title of journal
		Gauderman – Title of journal
		Gehring – Title of journal
		Geroulakos – Title of journal
7-144		Gotschi – Title of journal
		Geenland – Title of journal

		Grigg – Reference
		Gabelova – Title of journal
		Gabelova – Title of journal, “Farmer Peter B” should be written “Farmer PB”.
		Ha – Title of journal
		Haland – Title of journal
		Hashimoto – Title of journal
		Heinrich – Title of journal
7-145		Hiramatsu – Title of journal
		Hollander – Title of journal
		Iba – Title of journal
		Ishibara – Title of journal
		Izawa – Title of journal
		Jacobsen – Title of journal
		Jalaludin – Title of journal
7-146		Janes – Title of journal
		Janssen – Title of journal
		Khattar – Title of journal
		Kizu – Title of journal
		Knobel – Title of journal
		Kunzli – Volumen and pages
		Kunzli – Title of journal
		Lacasana – Title of journal
7-147		Loomis – Title of journal

		Lund – Title of journal
		Maheswaran – Title of journal
7-148		Matsumoto – Title of journal
		Miller – Title of journal
		Nordling – Title of journal
7-149		O'Leary – Title of journal
		O'Leary – Title of journal
		O'Neill – Volume and pages
		Oftedal – Title of journal
		Oftedal – Title of journal
		Parker – Title of journal
		Pedersen – Title of journal
		Pignoli – Title of journal
		Pires-Neto – Title of journal
7-150		Pope – Title of journal
		Pope – Title of journal
		Resnick – Title of journal
		Ritz (2008) – Title of journal
		Ritz (2006) – Title of journal
		Ritz (2000) – Title of journal
		Rogers – Title of journal
		Rojas-Martinez – Title of journal
7-151		Rosenlund – Title of journal
		Schatz – Title of journal

		Schindler – Title of journal
		Sharma – Title of journal
7-152		Shinkura – Title of journal
		Somers – Title of journal
		Song – Title of journal
		Sorensen – Title of journal
		Sram – Title of journal
		Suh – Title of journal
		Sun – Title of journal
7-153		US. EPA (2005) – "Just" is hanging. What does this mean?
		U.S. EPA (2006) – Correct "AGency".
7-155		Yauk (2008) – Reference
		Yauk (1996) - Reference
		Yoshida – Title of journal

Cowling Comments (Dr. Ellis Cowling)

Charge Question 1:

> Welfare effects evaluation in Chapter 9: Several revisions were made to the evaluation of the welfare effects evidence in Chapter 9, in response to the CASAC PM Panel comment, to focus further on effects on climate and ecosystems and include further evaluation of urban visibility evidence, where possible. In addition, as recommended by the CASAC PM Panel, key findings and conclusions from this chapter were incorporated in Chapter 2. The discussion of PM effects on climate was increased with substantially more detail from recent publications, including discussion of specific climate forcing effects from individual PM components and size fractions. The discussion of ecological effects was also reorganized to focus on the types of effects and effects of individual components. For the effects of PM on visibility, new material was added including sections on direct optical measurements and the value of good visual air quality. Please comment on the effectiveness of the reorganization and revisions regarding welfare effects.

I was pleased with the adjustments in organization that were achieved in this second draft ISA for PM and with the statements of key findings with regard to public welfare effects in Chapter 2.

I was even more pleased to find that a reasonably very well-balanced distribution of attention was given in Chapters 2 and 9 of the PM ISA to three of the four types of welfare effects of PM – with visibility effects being covered in the first 83 pages in Chapter 9, climate effects being covered in the next 104 pages of Chapter 9, and ecological effects being covered in 43 pages in Chapter 9 (recognizing, of course, that the very substantial ecosystems effects the PM forms of airborne NOx and SOx on acidification, nutrient enrichments, and methyl-mercury enhancement are being handled very thoroughly in the separate integrated NAAQS assessment document for public welfare effects of NOx and SOx.

It was somewhat disappointing, however, to discover that a pretty skimpy 6 pages in Chapter 9 and only three short paragraphs in Chapter 2 is all the attention that was given to the materials damage effects of PM. I would have expected that soiling of exposed textiles and the painted and exposed stone and other surfaces of buildings and monuments would have deserved somewhat more attention.

Frey Comments (Dr. Chris Frey)

Charge Question 5: *Integrative Synthesis in Chapter 2: The CASAC PM Panel recommended expanding Chapter 2 to include all important findings of the PM ISA. The integration of health evidence in Chapter 2 was reorganized to focus on effects of $PM_{2.5}$, $PM_{10-2.5}$, and ultrafine particles, and was expanded to include discussions of effects for which a "suggestive" causality determination was drawn. New integration sections were added that combine the evidence for health effects of $PM_{2.5}$, $PM_{10-2.5}$, and ultrafine PM across exposure durations. In addition, these integration discussions incorporated evidence related to mode of action, dosimetry, atmospheric chemistry, and exposure assessment to the extent possible. When appropriate, figures were added that summarize the overall U.S. and Canadian epidemiologic evidence for specific size fractions and exposure durations, along with the concentrations reported in the studies or provided by study authors. A new section was also added to Chapter 2 that contains policy-relevant considerations, including summaries for the evidence for susceptible subpopulations, lag structure of associations in epidemiologic studies, and the PM concentration-response relationship. Please comment on these revisions and additions to the integration of health effects evidence in Chapter 2.*

Response: The integration of health evidence and its organization with respect to effects of $PM_{2.5}$, $PM_{10-2.5}$, and UFP is extremely helpful to the reader. The discussion of health effects endpoints for which a "suggestive" causality determination was drawn is helpful and appropriately fits in this chapter. The material on evidence for health effects of $PM_{2.5}$, $PM_{10-2.5}$, and UFP for long- and short-term exposure durations is important to the chapter.

The graphical summary (Figure 2-1, and Figure 2-4) of U.S. and Canadian epidemiologic evidence is good. The discussion of policy-relevant considerations is helpful. Overall, the structure and content of Chapter 2 is very good.

A few specific comments are offered.

Page 2-4, line 8. What averaging time is the basis for these “average” concentrations?

Page 2-5, line 18. “maintained” is not the right word. Could delete “maintained at”

Page 2-9, line 7. EGUs are point sources with stacks, so it would be more clear here to refer to “non-EGU point sources,” if that is the intended meaning.

Page 2-10, line 14. Use “such as” rather than “like”

Page 2-13, lines 5-20. For clarity, should explain why PM_{10} is not separately considered, just to avoid confusion on the part of some readers who might be expecting to see $PM_{2.5}$ and PM_{10} as the focus, since these are the indicators of the current standard.

Page 2-13 – last half. As a rhetorical device, it is weak to start out with negative findings or what is not known. Also, it would help to have just one table that summarizes for each size range the list of health effect outcomes and the causality determination. As a reader, I would prefer to first see a list of the key outcomes that are the focus of the ISA, followed by a list of those for which there is inadequate evidence.

Page 2-16, line 1. The word "precise" is used here and in a few other places. However, the intended meaning might be "statistically significant" rather than "precise." Either change the term here or define what is meant by "precise."

Page 2-24: this page seems to go into a lot of detail to a depth that is not consistent with the rest of the chapter. Perhaps cut back on this, and just make key points.

Page 2-25. Similar comment. Reader is wondering what is the "bottom line" here? Details are in later chapters. However, the last paragraph on this page is very good.

Page 2-30, line 14. Delete "It is also important to note that". More importantly, what are the implications of this paragraph? This paragraph is descriptive but it is not explained as to the significance or implications of what is being described.

Page 2-33, line 11, this is awkward. "studies" are inanimate and cannot attempt to do anything. This section needs copy editing.

Page 2-34, line 32-35. "various" might more accurately be replaced with "particular." The term "susceptible" is used here but is not defined. The first time that the terms "susceptible" and "vulnerable" are used (either in Chapter 1 or this chapter) they should be defined briefly, with a reference to the later section where they are discussed in more detail.

Page 2-42 - top of the page. Is PM size a factor?

Page 2-42, lines 15-17. This text refers to "effects" on climate. In the context of all other effects discussed throughout the document, the presumption is that they are adverse effects. In this case, it is not clearly stated as to whether the "effects" are adverse or beneficial, and hence the policy implications of this statement by itself are unclear.

Grantz Comments (Dr. David Grantz)

ISA for PM, 2nd External Review Draft

Comments by David Grantz on Charge Question #6—Welfare Effects

Overall

I was very pleased to read this second draft ISA. The authors have paid close attention to the concerns of previous reviews. The resulting two chapters of concern here, Chapters 2 & 9, are well organized (few comments below) and provide a useful compendium of available knowledge from the previous CD and more recent literature. The current Chapter 2 contributes significantly to the presentation. Very few issues of interpretation remain, and these are addressed below.

The increased attention to climate change is appropriate and generally well done. As noted below, there is some confusion in the discussion of PM impacts on photosynthetically active radiation (PAR). Briefly the issue is that photosynthesis per leaf responds nearly linearly to PAR up to some near-saturation flux. At this flux it becomes useful to spread that (excess) radiation around to lower leaves which (due to shading of direct beam radiation by upper leaves) are generally still on the linear portion of the PAR response curve. Diffusion by PM accomplishes this spreading around of PAR. If PM reduces total PAR below saturation for the upper leaves, diffusing the flux will have only minimal and second order impacts on total plant photosynthesis. Also, once diffuse radiation has become a significant fraction of total PAR, then further increase in PM will reduce plant photosynthesis by decreasing total PAR. The current text is unclear and seems to imply a conflict or conundrum that does not exist. The issue is important because it lends itself very well to the ultimate goal of modeling of response-exposure relationships to PM.

I remain disappointed that there is little attempt to link ecological endpoints to specific levels of ambient PM, with a view towards moving the debate towards response-exposure relationships. In several cases cited there are clear endpoints, and exposures are documented. The studies of Regoli et al. 2006 with snails and Kuki et al. 2009 with plants, as examples, seem to demonstrate causality and at least the beginnings of such relationships. Reference to the study of Nash, 1975 (page 9-235, line 34) seems to best approximate this goal. Overall, the current organization of Chapter 9 by component works very well.

Specific Comments

Chapter 2--*Substantive comments*

page	line	Comment

2-3	25	It is important to define UFP (ultrafine particles) at first use, with respect to size and mode of origin. This might be accomplished by moving all of Section 2.1.5 (on PM Formation and Removal) into this introductory location, as a way to introduce and define PM.
2-4 2-5 2-12	14 25 14-21	The commonly understood more rapid deposition of coarse PM is initially stated, but this contrasts with later references to the very rapid disappearance of UFP. This should be explained (ie. is UFP growing out of the class or depositing out of the atmosphere?)
2-6	14	Is the afternoon peak of UFP also due in part to the collapse of the boundary layer as in line 8, just above?
2-6	32	Might want to explain why this logical association between fine PM and O3 was not observed in these three cities.
2-6	33	Section 2.1.4 on Measurement Techniques may not be required at all in this summary chapter.
2-9	1-4	The implications of this first half of the paragraph are not clear. Perhaps this should be merged into Section 2.2.1
2-11 2-12	14, 27-30 *23*	Define first use of "ambient" in this context, is it in opposition to regional or to indoor or to personal?
2-14 2-26 2-31	*titles*	These section headings might better be titled "Effects" rather than "Exposure". Also these sections (especially 2.3.1) may have too much detail for this summary chapter.
2-14	*Table 2.1*	Seems odd that many of the CV endpoints were death, but CV is "causal" and mortality is only "likely to be causal"?
2-20 2-28 2-32	*Sections 2.3.2* *2.3.4* *2.3.6*	These sections seem redundant in an already 'overview' chapter. In particular, section 2.3.2 contains much of the information that is required in chapter 2. Perhaps these summaries can be blended into their preceding sections and condensed.
2-30	*22-23*	Text states "is associated" when it was concluded "is suggestive…". These are not equivalent.

2-37	*Sect 2.4.3*	This entire section is cumbersome and unclear. A figure illustrating the no threshold log-linear relationship for some endpoint could be placed here (and in section 6.2.10.10 where it is also lacking).
2-38	*7*	Add "including NOx and Sox" between "airborne PM" and "on visibility". The distinction between the PM document and the NOx-Sox document will confuse many readers and should be made very clear every time it comes up.
2-43	*5-12*	The relationship between crop growth and total intercepted PAR, and the role of diffuse PAR when upper leaves are light saturated, is poorly conveyed here and in the relevant parts of chapter 9. This is an important point, that if properly explained the first time would obviate much later discussion and remove the apparent conflict with data showing that increasing PM both increases plant growth due to light scattering and decreases it.

Chapter 2--*Other comments*

page	line	Comment
2-4	5	This summary statement leaves the impression that nothing can be known. A more positive concluding sentence here, perhaps considering the importance of regional averages, and the existence of local hot spots, and more accurately summarizing the subsection, would be helpful, particularly for readers who may only read this chapter.
2-4	8	Should specify the averaging period (is it as specified at 2-5, 29 or at 2-14, 5?)
2-5	21	need a summary statement here
2-7	28	"isoprene" seems to be in the wrong place.
2-8	18	farm equipment may be even more confounded with trucks than are locomotives.
2-9	23	should indent new paragraph

2-14	*14*	Reference to null findings is unclear and potentially confusing
2-15	*3*	Might define "vasomotor" for general readers
2-20	*9-10*	Methylation is not a change in the genome
2-31	*4*	Typographical error in "cardiovascular"
2-36	*13*	Missing word before "children"
2-36	*22*	"result(s)"
2-36	*25-26*	*a priori* should be italicized
2-39	*27-29*	Is carbonaceous PM largest only in the West, needs to be clarified.
2-41	*7-8*	There should be a formal reference to the IPPC AR4.
2-42	*9-14*	This run-on sentence is hard to interpret.
2-43	*32-34*	The sentence is poorly constructed and factually unclear. Possible solution is to insert "which are more often deposited by wet deposition" between "fine particles" and "are more likely to contain"

Chapter 9--*Substantive comments*—line numbers are approximations

page	line	Comment
9-2	*21-22*	"Biogenic" combustion should be "biomass" combustion. If prescribed burns are "natural" from a regulatory perspective then this requires a brief explanation.
9-8	*1-31*	The level of detail on dark visibility is not necessary here, as it is ultimately dismissed. Perhaps this section could be moved to later in the chapter, as a suggestion of future concerns.
9-40 9-43	31 Fig. 9-22	The text refers to Puerto Rico values of fine soil, but the figure appears to indicate no data for Puerto Rico.

9-46	Fig. 9-24	San Joaquin Valley data are unclear. This is a nearly closed airbasin, unlike South Coast. Text is needed to explain what is the source of regional PM (i.e. what is the region), and where local PM was measured (just in urban Fresno?). Given internal gyre based circulation in this basin it is not clear that the Valley itself constitutes a truly regional source, nor that offshore sources are dominant as implied on 9-54, 28 and on 9-55, 1to29. There seems to be a general confounding of South Coast and San Joaquin Valley. An explicit analysis similar to that provided for the Columbia Gorge (9-57, 1to5) would be useful.
9-93	20	Maximum sight distance of 8 km in Washington DC is outside the range of visibilities presented (Table 9-2), does this require some explanation?
9-102	25 on	The source of NOx to support the Midwest nitrate bulge has not been well discussed to this point, and should be here. Ammonia has been dealt with adequately.
9-210	21	PM effects on precipitation have been omitted from section 9.3.10 and should be considered here.
9-213	6-7	The concluding sentence of this paragraph does not summarize the paragraph, and may belong with the following paragraph. The appropriate concluding sentence here should summarize the preceding CD and the material to be excluded from the current ISA.
9-221	3	There is a distinction made between uptake (or maybe just response?) at the air-plant interface, and uptake by above ground tissue. This is hard to understand. The authors may want to consider citing a description of these processes, and of the leap-frog behavior of SOCs discussed later, in the review by Krupa et al., 2008, Journal of Air and Waste Management Assoc 58: 986-993. This reference has not been cited and perhaps should be consulted. This reference could be useful at p. 9-226 mid page, p. 9-256, bottom, and p. 9-259, mid page.
9-221	13	Scavenging by the snowpack implies only dry deposition. There may also be wet deposition in the falling snow.
9-226	7-17	This paragraph takes a generally positive view of biomonitoring using mosses etc., which contrasts with conclusions on p. 224-225.

		These sections should be more closely aligned with each other.
9-227	8-15	There are some important concepts contained in the previous CD regarding deposition, including specific cation depletion with depth and distance into forests, that should be reviewed here. The material at top of 9-236 on mosses and lichens should be incorporated into this section. These data form the basis for existing models, and for the criticism of them posed by Pryor and discussed here. In general, this paragraph is hard to understand and should be revised. An entirely new idea is introduced with "condensation processes…". This sentence should start a new paragraph, but more importantly should be integrated with the overall theme of this section, which has to do with the appearance and disappearance of PM in canopies.
9-227	16-22	This paragraph requires some revision to better communicate that biomonitoring and ecosystem impact are different endpoints. The sentence "As an ecosystem pool…mosses" could perhaps be moved to the end of the paragraph.
9-231	10	Only near the coast is most salt from sea salt.
9-231	21-28	This paragraph is out of place. It might be inserted near the beginning of 9.4.3.1. The last sentence, "Fine particles…demonstrated" should be moved to the bottom of page 9-229.
9-234	1-8	The material currently in 9.4.5.4 could be included here. Throughout the metals section there is some blurring of direct and indirect effects that should be clarified.
9-235	24	It would be useful to explore how *S. terebinthifolius* avoided stress since this would be a useful attribute to look for in other systems. As currently written this statement does not communicate much.
9-246	3-6	The discussion of loss of peat and increase in Hg should be moved to or summarized in the section on climate change.
9-247	24	First paragraph of 9.4.5.5 seems to imply that these are toxicity issues ("metals in PM deposition limit phytoplankton growth"), but actually they are fertility issues and positive effects.
9-252	22-25	The dependence of uptake on solubilized Cd is reasonable, but this begs the question what determines solubilization (redox, acidity, ?)

9-253	32-36	While the effects of Cu and Ni may be solely attributed to their toxicity as statedhere, it was implied previously that these heavy metals displace from soil exchange sites the very cations (Mg, Ca and Mn) that are reported here to be depleted. Both inhibition of uptake and depleted soil stores may be at work.
9-258	20-24	The greater content of PAH in littoral than pelagic species may reflect sequestering in sediment as indicated, or it may (also) reflect differences in diet of the two communities.
9-259	5-8	The role of elevation does not seem to justify use of salmonids as a biomonitor. I suspect there was some linkage to prevailing PM concentrations (which may have also varied with elevation?) in the original publication which could be discussed here.
9-262	1-10	Again, discussion of PAR and diffuse light requires some attention. Also haze has been "modeled" or "calculated" or "measured" rather than "estimated" (to diminish visible radiation).
9-267	4-8	Rust generally applies to iron oxide. Whereas such coatings on aluminum do provide some protection against further corrosion, iron oxide does not, due to its flaking behavior.
9-267	16	Is this really dry deposition of gypsum (CaSO4) or is it formation in place when sulfuric acid meets limestone or marble?

Chapter 9--*Other comments*—line numbers are approximations

page	line	Comment
9-1	*18*	Insert "including NOx and Sox" between "PM" and "on visibility"
9-13 9-24	*Eq. 9-1* *Eq. 9-2*	The RH functions shown at top of page 9-14 could be placed within equation 9-1, as "where" statements. Analogous RH functions should be described for equation 9-2.
9-49	8-9	The sentence, "Note that the concentration…trend line slope" could be moved to the figure legend.

9-61	Fig 9-32	It is unclear what the sulfate and nitrate concentrations in the individual figure legends refer to.
9-64	Fig 9-34	Is top panel average of Class I areas as indicated in figure, or only Yellowstone NP as indicated in the legend?
9-72,3	Figs 9-38,39	Scale is not technically unitless as indicated in legend (it is %).
9-96	26-33	The deciview units should be translated into visual range, as was done above.
9-213	29	The reference to Odum 1985 is not complete (p. 9-292)
9-222	20	The distinction between combustion sources and petrogenic sources is unclear. Does combustion source refer to biomass combustion?
9-235	15-17	Sentence beginning, "A greenhouse study…" is confusing. There is a word missing ("under"?) prior to "simulated".
9-237	22-26	Second half of paragraph, "Sequential extractions…unavailable" could be incorporated into the beginning of this section 9.4.5.2.
9-242	22	In line beginning with "by increasing" there is a critical typographical error, "creasing Cd uptake". Is is increasing or decreasing? Also at beginning of next paragraph "mycorrhizae" is misspelled.
9-243	8-11	The discussion of shallow-rooted species is not very useful, and should be deleted as a distraction.
9-250	7	MADE should be AMDE. It would be useful to define the reactive gaseous Hg species of interest here.
9-251	7	Should include cement factories as sources of metals, given earlier citation of Massicote et al., 2003 to this effect.
9-252	1-5	It would be useful to describe briefly how isotopes of C and N can demonstrate biomagnifications of metals. In the second paragraph, the lack of biomagnifications in aquatic systems, if generally true, is sufficiently counterintuitive that it should be explained a bit more.
9-256	25-33	The first 6 lines of this paragraph should be moved to the earlier section on deposition.

9-261	18	Ecological effects also include changes in soil microbiology, which should be added to the list at the beginning of section 9.4.7. In the second paragraph, ions should be added to the list of constituents with ecological effects.

Helble Comments (Dr. Joseph Helble)

Charge question 4, ISA

Revisions to Chapter 3 on Source to Exposure: Consistent with revisions made to the health effects chapters, Chapter 3 was revised to clarify that PM10 incorporates both PM2.5 and PM10-2.5 and reorganized to begin with PM2.5 and PM10-2.5, followed by PM10, where applicable. The discussion of measurement techniques and chemistry of PM10-2.5 has been expanded in Sections 3.4 and 3.5, in response to CASAC comments. In addition, Section 3.8 on human exposure to PM has been reorganized and expanded to better characterize the evidence and provide useful information for interpretation of epidemiologic studies. We would appreciate comments from the CASAC PM Panel on these revisions.

Summary

The expansion and reorganization of Chapter 3 now provide a generally clear, well-organized, and comprehensive review of $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10}. The sequencing of discussing PM2.5 followed by the successively larger size fractions provides a logical framework for addressing the important differences among these size classes. The revised chapter also does a good job, overall, of summarizing areas where studies suggest differing trends, and identifying areas where data are sparse and additional research is needed.

The reorganization and expansion specifically to address deposition in more detail, measurement techniques, and diesel emissions were generally clear and well-structured. With regard to deposition, a minor suggestion is that Section 3.3.4 page 3-21, the general introduction, be expanded to address wet deposition. It is meant to be a general overview of deposition, but only discusses dry deposition and ignores wet deposition other than a passing reference in the first sentence. Organizationally, if this is to function as the introduction to the sections providing a more detailed discussion of both wet and dry deposition, an overview of wet deposition needs to be added.

The importance of particle morphology was clarified in this draft (pages 3-6 to 3-7) as requested in the last review, but the discussion remains a general one. There is some limited literature on surface area, for example, that could be considered.

The embedded links to reference documents are a very welcome feature.

Detail Comments

Lines 19-20, page 3-7, states that "particles in ambient air are generally mixtures or agglomerates of particles…from multiple sources…" This statement is true if one is referring to condensed or adsorbed species on the surface of nearly all PM, but otherwise, this statement is misleading because it is dependent upon particle size and proximity to source. This statement should be clarified or, better, removed.

In the discussion of county-based PM spatial distribution in section 3.5.1.1, a slightly expanded discussion of the completeness criterion would be helpful in interpreting the results. Counties appear in white in the associated figures when they fail to meet the 75% completeness criterion. Failing to meet this criterion could, however, be a result of a lack of appropriate monitoring sites within the county, or a failure to obtain adequate (complete) data from appropriate monitoring sites. Parsing this would be helpful – i.e. how many of the counties failed to meet the criterion because existing monitoring sites did not report sufficient data?

Organizationally, it isn't clear that the summary in section 3.5.4 is necessary. The individual subsections in section 3.5 provide a detailed review of the data, and the summary is essentially repeated in section 3.9. Section 3.5.4 therefore adds little. To shorten the document, this sub-summary, as well as a few other sub-summaries at the end of individual sections, could be deleted, with section 3.9 serving as the overall summary for Chapter 3.

Page 3-225, line 28 – it seems that two different sentences, and two different ideas, run together in this line. The first part of line 28, and the text that precedes it, appears to focus on automobile indoor exposure. The remainder of the paragraph, with no transition, addresses school buses. Were parts of two different paragraphs truncated?

<u>Minor / Editorial</u>

Figure 3-2 additional detail needed regarding sampling location and sampling details.

Lines 10-11, page 3-16 – first sentence in the paragraph confusing. Substitute "being emitted" for "emission" to clarify.

Lines 16 and 17, page 3-31 – impaction-based collection efficiency will decrease, not increase, as dp decreases.

Line 5, page 3-34: "monvolatile" should be changed to "nonvolatile"

Line 14, page 3-45: change "detect" to "detecting"

Line 20, page 3-45: change "media" to "medium"

Tables 3-3:, 3-4, etc. add commas to N values so magnitude of population figures more easily seen

Figure 3-7 and 3-8: display would be enhanced by showing PM2.5 and PM10 monitors on the same figure

Line 6 page 3-59, fix font on PM2.5. Similar comment lines 8 and 9, page 3-60

Line 31 pg 3-70, insert "per" before cm^3

Figures 3-12 to 3-14: did EPA consider plotting these figures without using different sizes for the different concentrations (i.e., using different colors only)? It might make the figures easier to read.

Figure 3-19 and similar figures – adding state borders would facilitate a quicker understanding of monitor locations

Lines 10 and 11, page 3-135: figure numbers should be changed to 3-52 and 3-52

Table 3-17 is not adequately explained in the text nor the caption. The parenthetical values in column 2 need to be described, and the basis for the data (ng/kg of what? presumably emitted PM) stated explicitly. Also, while it is likely that this table came directly from the cited source, is EPA certain that 5 significant figures (seen in several of the table entries) are justifiable?

Line 10, page 3-144: "mighty" should be changed to "might"

Line 8 page 3-151, "much" should be changed to "must"

Figure 3-65, page 3-165: caption is incomplete

Figure 3-68 caption – symbol □ is missing. Also missing from title of Table 3-19 page 3-187, and from titles of Tables 3-20 through 3-23

Figure 3-73 page 3-174: caption, change "theem" to "them"

Line 10, page 3-215: "In this work," - ? Incomplete sentence

Line 20, page 3-215: complimentary should be complementary

Lines 10-11-12 page 3-237, sentence would read better as opening to section. It does not follow as a conclusion.

Page 3-246, Low Angeles should be Los Angeles

Henderson Comments (Dr. Rogene Henderson)

Reply to Charge Question #3; Susceptible Populations

I found Chapter 8 to be complete, clear and well-organized. The authors have been responsive to the CASAC critique of the first draft of the chapter. Their definition of "susceptible" is clearly stated and there is a rather complete listing of how the term has been used in the literature in the past.

Table 8-2 introduces all of the susceptibility factors that have been evaluated, as well as the size fraction evaluated and the length of the exposures. The table is then followed by a more detailed description of the evaluations that were made. This is an appropriate organization, with one exception. The introductory table 8.2 does not have a column indicating the results of the evaluations. Thus if one only looks at the table, which is titled simply "Susceptibility Factors," one might get the impression that all of the listed factors showed a susceptibility, when some factors, such as gender, did not. I recommend at least expanding the title to "Susceptibility Factors That Have Been Evaluated," and if possible add a column that suggests what the results of the evaluation were. Maybe just a plus/minus approach could be used.

1) I found Chapter 8 to be complete, clear and well-organized. The authors have been responsive to the CASAC critique of the first draft of the chapter. Their definition of "susceptible" is clearly stated and there is a rather complete listing of how the term has been used in the literature in the past.

2) Table 8-2 introduces all of the susceptibility factors that have been evaluated, as well as the size fraction evaluated and the length of the exposures. The table is then followed by a more detailed description of the evaluations that were made. This is an appropriate organization, with one exception. The introductory table 8.2 does not have a column indicating the results of the evaluations. Thus if one only looks at the table, which is titled simply "Susceptibility Factors," one might get the impression that all of the listed factors showed a susceptibility, when some factors, such as gender, did not. I recommend at least expanding the title to "Susceptibility Factors That Have Been Evaluated," and if possible add a column that suggests what the results of the evaluation were. Maybe just a plus/minus approach could be used.

Hopke Comments (Dr. Phil Hopke)

Chapter 3

This chapter is in generally good shape. I think there are some minor changes noted below that will improve it.

There are a number of cases where they talk about "accuracy" with respect to sampling or determination of concentrations. In most cases, there is absolutely no knowledge of accuracy since there is no way to provide a truly known standard to which the measurement can be compared. There may be systems with good precision, but there are no deployed system with know accuracy. Thus, there needs to be a careful review of the use of "accurate" with respect to the description of any ambient measurement.

Primary vs secondary organic aerosol:
I suggest it would be very helpful to clearly distinguish the various types of organic carbon species associated with airborne particulate matter. It is too simplistic to just classify the OC into primary and secondary. There is also oxidized primary organic matter. The problem is the oxidized POM will also be water soluble and have the general characteristics of SOA. However, given the sources are different and the chemistry is entirely heterogeneous, it is important to clearly distinguish these three different portions of the particulate organic matter. The process of forming SOA or oxidized POM leads to the formation of oxidizing species (reactive oxygen species). This source of exogenous ROS could be important in the induction of adverse health effects. Thus, connecting SOA formation with high concentrations of ROS such as seen by Docherty et al. (Docherty, K. S., Wu W., Lim Y. B., Ziemann P. J. (2005) Contributions of organic peroxides to secondary aerosol formed from reactions of monoterpenes with O_3, *Environmental Science and Technology* 39, 4049-4059). Thus, we can expect ROS to be associated with ambient particles and that has been observed by multiple groups (Hung, H-F., Wang, C-S.(2002) Experimental determination of reactive oxygen species in Taipei aerosols. *Journal of aerosol science* 32, 1201-1211; Hasson A. S., and Paulson S. E. (2003). An investigation of the relationship between gas-phase and aerosol-bourne hydroperoxides in urban air, *J. Aerosol Sci.*, 34: 459-468.; Venkatachari, P., Hopke, P.K., Brune, W.H., Ren, X., Lesher, R., Mao, J., Mitchell, M. (2007) Characterization of wintertime reactive oxygen species concentrations in Flushing, New York, *Aerosol Science and Technology*, 41, 97-111; Venkatachari, P., Hopke, P.K. ,Grover, B.D., Eatough, D.J.(2005) Measurement of particle-bound reactive oxygen species in Rubidoux aerosols, *Journal of atmospheric chemistry*, 50, 49-58). Thus, there needs to be a short paragraph added to point to this pathway to the formation of a potentially important class of atmosphere aerosol species that could be directly related to observed human health effects.

Other major issues:

Although past the cut-off date for inclusion, it may be useful to note Amato F., Pandolfi M., Escrig. A., Querol. X., Alastuey A., Pey. J., Perez N. and Hopke P. K., *Atmospheric Environ.* 43: 2770-2780 (2009). This paper demonstrates how known source profiles can be included within the PMF framework and yield an improved source resolution.

The description of PLS on page 3145 is not fully correct. PLS is in fact a biased regression method that is really designed for prediction and not for explication as is the goal of receptor modeling. In addition, there is really no basis for choosing PLS over other prediction methods like principal components regression (PCR). It is really not a receptor model and it is not clear it really belongs in this section.

There are some minor issues to be resolved.

On page 3-4, the table uses the term "condensation of gases." Gases do not condense at normal temperatires and pressures. The correct term here is condensation of "vapors."

Chapter 5
The discussion in section 5.1 only focuses on endogeneous ROS. It should be recognized that there is exogenous ROS associated with the ambient particulate matter to which we are continuously exposed. Even in the evening, there is still significant particle-bound ROS and thus, it should be noted as part of the total dose of ROS to the tissue.

Lippmann Comments (Dr. Mort Lippmann)

Post-Meeting Review Comments

General Comments:

1) I commend the organizers and authors of this document for providing the CASAC PM Panel with a well organized and readily readable text that is, for the most part, thorough and accurate in its presentation of the peer-reviewed literature most relevant to Standard setting for PM.
2) I have one **major disagreement** with the authors in terms of their characterization of Health Effects (Section 2.3). Specifically, in Section 2.3.1.2 on Effects of Long-Term Exposure to $PM_{2.5}$, the conclusion that **"a causal relationship is likely to exist between long-term exposure to $PM_{2.5}$ and mortality"** is insufficient. It should be changed to **"a causal relationship exists between long-term exposure to $PM_{2.5}$ and mortality"**. How is it possible to conclude that **"a causal relationship exists between long-term exposure to $PM_{2.5}$ and cardiovascular effects"** (page 2-18, lines 8 & 9), and that the strongest support for that causality determination comes from the associations of ambient PM2.5 and annual mortality, and then equivocate on the conclusion that $PM_{2.5}$ causes excess mortality. The document amply showed that cardiovascular mortality accounts for most of the excess mortality (Pope et al. 2004). The conclusion that I challenge is apparently drawn, for the most part, from Section 7.6.5, in which it failed to properly consider that chronic $PM_{2.5}$ exposure studies in mice caused exposure-related aortic plague progression. This research provides a toxicological basis for supporting the epidemiological findings of excess cardiovascular mortality and a causality conclusion.
3) I have an important **organizational comment** on the draft ISA. It is inappropriate to include the summary and synthesis on associations of PM sources and components with health effects only in Chapter 6 on short-term exposures, since it covers the literature on both short-term exposures and long-term exposures, the latter being relevant to Chapter 7. This topic should be a separate chapter. If this is not possible, the topic should be covered in both Chapters 6 & 7.
4) There seems to be an overemphasis on UFP, especially in Chapter 5, where the potential to cause adverse effects is so prominently featured, along with the implication that particle number concentration is the most important metric for risk. Some additional discussion of the fact that supporting evidence for this hypothesis remains weak is warranted.
5) Some generic changes that should be made for the final version are:
   a) Use a consistent criterion for "recent". In the context of this document it should refer to papers appearing since the closure on the last PMCD;
   b) Italicize *in vivo, in vitro, in situ, a priori*, etc.

Specific Comments:

PAGE	LINE	REVIEW COMMENTS
1-3	1 and 2	Two lines of text were left out here
1-17	9-12	It is inappropriate to include a summary and synthesis on associations of sources and components with health effects in Chapter 6, since it covers both effects of short-term and long-term exposures. It needs to be a separate chapter, or divided into parts for Chapter 6 and parts for Chapter 7.
1-24	15	Insert "sizes, respiratory parameter and" before "branching"
1-24	34	Citations to the concentrators developed and used by the Harvard Group need to be added here
2-31	5	I don't agree with the statement: "fresh DE, which is typically dominated by UFPs". It may be true for the number concentration, but is usually not true for mass concentration due to rapid coagulation of the UFPs before they are inhaled.
3-111	1-14	Cite work of Peltier et al (in press) and Peltier and Lippmann (in press) on intra-urban variations in N and V in NYC
4-1	26	Insert "Substantial" before "exposures"
4-1	30	Change "frequently" to "can"
4-2	2	Change "Fibers, therefore, deposit largely" to "fibers longer than 10 µm can deposit"
4-2	6	Insert "long" before "fibers"
4-2	6	Change "prevent" to "affect"

4-3	28	Change “airways” to “respiratory tract”
4-3	29	Change “airways” to “respiratory tract”
4-5	2	Change “rats” to “rodents”
4-6	25	Change “scintigraphic” to “external measurements of retained particles having radioactive tracers”
4-6	25	Change “These” to “Scintigraphic”
4-14	17	Insert “anatomical and” before “ethical”
4-15	12	Add “and nasal vs. oral breathing” after “size”
5-1	18	Insert “with the exception of ultrafine PM” before “There”
5-2	Fig. 5-1	Lowest oval is mis-labeled. It should refer to *in-vivo* responses, rather than cellular system assays.
5-2	Fig. 5-2	
5-3	21	Insert “soluble” before “metals”
5-8	13	Change “$PM_{2.5}$ “ to “accumulation mode PM”
5-27	15	Delete “ultrafine”
6-4	12	Change “m” to “ms”
6-17	7	Change “Tuxedo” to “New York”
6-17	25	Change “of” to “in”
6-95	15	Change “NA^+” to “Na^+”
6-103	Fig. 6-2	Show vertical line at 0 change
6-250	Sect. 6.4.1	Chen & Schwartz (2009) does not belong here it is clearly a study of chronic exposure and effects
6-251	Sect. 6.4.3	Cite Veronesi et al (2005) in this section. (See ref. listed at end of my comments).
6-252	Sect. 6.4.3.1	Calderon-Garciduenas et al. (2003) does not belong here in the acute exposure section.

6-253	2nd and 3rd para.	These studies do not belong in the acute exposure section.
6-320	14	Change "correlation between each" to "correlations among the"
6-320	26	Change "inherently" to "sometimes"
6-321	16	Insert "and analyzed the concentrations of the components therein" after "CAPs"
6-325	12	Add citation to "Patel et al (in press)". (See ref. listed at end of my comments).
6-326	6	Insert "of" after "study"
6-326	3rd para.	What about the "Franklin et al (2008)" paper? It needs to be cited in this paragraph.
6-327	3rd para. Line5	Change "similar" to "simultaneous"
6-327	3rd para. Line7	Cite the "Sama et al (2007)" paper on the effects of CAPs on the liver here. (See ref. listed at end of my comments).
6-331	Table 6-17	Add another source category, i.e., "smelter effluent" , which is enriched in Ni, Cr, and Fe.
7-2	14	Cite Veronisi et al (2005) re: nervous system and Tang et al (in press) re: hepatic system
7-6	22a	Insert "$PM_{2.5}$" before "CAPs"
7-8	12a	Change "PM_{10}" to "Ambient Air PM"
7-10	Sect. 7.2.3	Create a new subsection on Epidemiology that cites the study of Chen and Schwartz (2008), using text from page 7-11, lines 4-6
7-25	9	Add at end of sentence: "and with $PM_{2.5}$- related plaque progression in chronically exposed mice"
7-30	3	"SAPALDIA" is mis-spelled
7-31	Table 7-3	Add descriptions of "Gent et al (2009) and Patel et al

		(in press) to this table
7-115	5	Add citation to "Xu et al (in press)
7-131	Table 7-9	Capitalize "New York City" in the table title
7-137	18	As noted previously, "likely to be" needs to be deleted

References cited in there Reviewer Comments

Chen, L.C, Quan, C., Hwang, J.S., Jin, X., Li, Q., Zhong, M., Rajagopalan, S., Sun, Q., Atherosclerosis lesion progression during inhalation exposure to environmental tobacco smoke in a susceptible animal model, and comparison with that occurring during exposure to concentrated ambient air fine particles. *Inhal. Toxicol.* (in press).

Lippmann, M. Semi-Continuous Speciation Analyses for Ambient Air Particulate Matter: An Urgent Need for Health Effects Studies. . *J. Expos. Sci. Environ. Epidemiol.* 19:235-247.

Lippmann, M. and Chen, L.C. Health effects of concentrated ambient air particulate matter (CAPs) and its components. *Crit. Rev. in Toxicol.* 39(10):865-913.

Patel, M., Hoepner, L.,Garfinkel, R., Chillirud, S., Reyes, A., Perera, F., Millrt, R. (2009). Ambient metals and elemental carbon in fine particulate matter predict wheeze and cough in very young urban children. *Am. J. Respir. Crit. Care Med.* (in press).

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.

Tan, H-H., Jinsheng, G., Fiel, M.I., Alvarez, C.E., Chen, L-C., Sun, Q., Friedman, S.I., Odin, J.A., Alina, J. Enhancement of fatty liver disease progression and TLR-4-dependent Kupffer cell activation by air particulate matter. *J. MOLEC. MED,* (in press).

Peltier, R.E., Hsu, S.i., Lall, R., and Lippmann, M. Residual Oil Combustion: A major source of airborne nickel in New York City. *J. Expos. Sci. Environ. Epidemiol.* 19:603-612.

Peltier, R.E., and Lippmann, M. Residual Oil Combustion: 2. Distribution of airborne nickel and vanadium within New York City. *J. Expos. Sci. Environ. Epidemiol.* (in press).

Xu, X., Kherada, N., Hong, X., Quan, C., Zheng, L., Wang, A., Zhong, M., Lippmann, M. Chen, L.C.. Rajagopalan, S., Sun, Q. Diesel exhaust exposure induces angiogenesis. *Toxicol. Lett.* (in press).

Malm Comments (Dr. William Malm)

Review of Integrated Science Assessment for PM

Page 9.3: The use of "transparency" is inappropriate here. It usually is reserved for a psychophysical reference of the "perceived" transmittance of the atmosphere. One could use "transmittance", but that would also be incorrect because contrast is dependent on other "stuff" besides transmittance. I suggest using physiochemical characteristics.

Page 9.5: The statement in the first paragraph is only true if certain scenic characteristics are met! "…regardless of background conditions" seems to say that a percent change in extinction exudes a similar perceptual response under all atmospheric conditions, which of course is not true.

Page 9.9: How about using "imperceptible" instead of "unperceivable"? "Achromatic" what? Should sentence read "…achromatic contrast and discoloration"?

Page 9.16: Should include some discussion of the level of uncertainty associated with nephelometer measurements of coarse particle scattering.

Page 9.21: "The resulting underestimation of total light extinction is typically much smaller since fine particle light extinction generally exceeds that contributed by coarse particles." Not true – coarse particle fraction of total scattering is often comparable to fine particle scattering.

Page 9.23: "Among the issues raised is that the algorithm tended to underestimate the light extinction for the haziest conditions that occur principally during the summer in the southeastern U.S. and overestimate for near pristine conditions that tend to occur most often in the arid western U.S." This statement is not generally true. In the sites where the IMPROVE algorithm underestimated extinction for the haziest conditions, it also overestimated extinction for the lowest extinction days. Generally, in the West the IMPROVE algorithm tended to work better than in the hazier eastern United States.

Page 9.82: It is well established that current regional scale models underestimate the SOA rather substantially. Model limitations should be discussed at some level before presenting modeling results. Also, it would be helpful to have a paragraph or two highlighting limitations and advantages in the various apportionment approaches. Something along the lines of:

> Transport regression receptor models are based on the association of source signatures with measured concentrations. Two different methods were employed in the RoMANS study. One method, trajectory mass balance (TrMB), used the residence time over defined source regions, estimated from RMNP back trajectories, to estimate the source signatures, while a hybrid approach developed source signatures from modeled concentrations of conservative tracers released from various source regions.
>
> In TrMB the model establishes a "scaling" factor between the residence time over a source region and the measured concentrations at the receptor site. Average emission, dispersion, chemical transformation, and deposition processes are incorporated into this one scaling factor. However, all of these processes vary with time, and the source apportionments derived from this technique are more accurate on the average than on an hourly or episodic basis. A statistical apportionment approach will inherently tend to overestimate those source regions where endpoints over the region are better correlated with measured concentrations, while underestimating those source regions where

endpoints over that source region show weak-to-little correlation with measured concentrations. Furthermore, air often arrives from two or more source regions simultaneously, causing the source signatures to be correlated, which increases the uncertainties in the analysis.

In the hybrid modeling approach, the apportionment analysis is more robust in that emissions and dispersion are explicitly modeled, and only chemistry and deposition are incorporated into the "scaling" factor. In both approaches the scaling factors account for possible errors in the models used to develop the source signatures, such as any systematic biases in the emissions used in the hybrid approach. Like TrMB, the apportionment estimates are more accurate on the average than for an incrementally small time period.

In reading the discussion of sources of ammonia and N_{ox} that contribute to particulate nitrate formation, it occurred to me that a discussion of the concept of partial scattering efficiency would be helpful, as first proposed by White. The concept being that the only meaningful way to look at scattering change response is to explicitly model the change in scattering resulting from a change in emissions. Of course, this assumes that the model captures all the complexities discussed in the pages presenting the nitrate apportionment work.

Page 9.89: Here, scattering as a function of emission change is presented. It would be helpful to have a discussion, as outlined above, of the concept of partial scattering efficiencies, including the limitations and advantages of approaching the apportionment problem in this manner.

Page 9.103: "Both are a product of incomplete combustion of fuels, including those used in internal combustion processes (gasoline and diesel emissions) and open biomass burning (smoke from wild and prescribed fire)." EC is more likely to be a product of incomplete combustion than OC. I don't think lumping EC and OC together as in the above statement is accurate. Much of measured OC is derived or SOA associated with VOC emissions, which can be natural or manmade.

Pinkerton Comments (Dr. Kent Pinkerton)

Response to Charge Question 3:

Susceptible Populations, chapter 8 in the Second External Review Draft of the Integrated Science Assessment for Particulate Matter, provides an excellent overview and summary of the current literature on this topic.

1) The majority of the definitions provided in Table 8-1 for the terms susceptible and vulnerable are appropriate, although it would be good for the authors to make some conclusion as to the most timely and relevant definitions for the purposes of this chapter.
2) The chapter discussion on epidemiologic, controlled human exposure, and toxicological studies with inclusion or highlighting of only those studies with stratified results to demonstrate susceptible populations is highly appropriate to allow for the comparison of subpopulations exposed to similar populations and using the same study design. The only concern for such comparisons would be the lack of personal monitoring to arrive at the appropriate conclusion of similar exposure conditions. Never-the-less, such comparisons of susceptibility based on factors of age, gender, race/ethnicity and pre-existing health conditions are critical and extremely helpful for presentation in this chapter.
3) Table 8-2 is a nice list of susceptibility factors along with exposure conditions (i.e. short-term or long-term) and the PM size fraction evaluated, but no explanation is provided as to the outcome and/or consequences of each susceptibility factor in terms of health endpoints. The authors should consider the addition of a column to briefly summarize the impact of each susceptibility factor on health impacts and/or observed health effects.
4) Inclusion of the hyperlinks to chapter 8 is a novel and extremely useful feature to the document to provide convenient and quick access to the database of scientific literature used by the USEPA. How often is this database (HERO) updated in view of the rapidly changing literature on PM and health effects? This is a wonderful addition to the REA!
5) The chapter subsections for each susceptibility factor listed in Table 8-2 are well-written and appropriate with corresponding hyperlinks to provide direct access to relevant documents under each topic. The authors should be commended for making these sections a pleasure to read and to comprehend.
6) Table 8.3 contains fascinating information on the percent of the US population with pre-existing cardiovascular disease (actual numbers are 51.6 million with hypertension, 24.1 million with heart disease, and 14.1 million with coronary heart disease), respiratory disease and diabetes. The table as well as the text for each of these conditions along with that of obesity emphasize the increased vulnerability of the US population to potential health effects of exposure to PM. It would be nice if the authors could provide some overarching conclusions for the relevance of these pre-existing diseases based on type and age for this section of the chapter.
7) Excellent summary for chapter 8.

Phalen Comments (Dr. Robert Phalen)

Chapter 1

The revision represents a significant improvement.

pg. 1-2, line 34: The last sentence is incomplete.

pg. 1-3, lines 5 to 8: Thank you for mentioning the "non-PM-exposure factor that might influence the association..."

pg. 1-12, lines 16-18: This looks like the cutoff date for cited literature. Is 5/09 a firm date for citing publications?

pg. 1-16, lines 13 to 16: It is good to see that "strength" of the evidence is considered, and also in Table 1-2 on "Aspects to aid in judging causality." The more I read on causality, the more I believe that the strength of an association is a key indicator of a true causal factor, as opposed to a surrogate exposure. When regulations are issued it is critical that the regulated pollutant is a true culprit. Much of the controversy, and opposition to PM NAAQS, seems to related to concern over whether particle mass is an appropriate indicator for health effects.

pg. 1-32, lines 5 to 11: There are several garbled words (typos) that need correcting.

pg. 1-33, line 3: The sentence is garbled.

pg. 1-33, line 9: Its "express", not "xpress."

pg. 1-34: Journal title missing from first reference:

Chapter 4

pg. 4-1, lines 23-26: Thanks for excluding fibers, nano-objects, etc. Inclusion of such unusual particles would expand the chapter unnecessarily.

pg. 4-3, lines 24 to 25: Please insert "small particles and small" before "aggregates", as large aggregates are not characterized by a "thermodynamic-equivalent size." Also, I would replace "thermodynamic-equivalent size" with "diffusion-equivalent diameter", in order to clarify and avoid confusion with the thermodynamic concepts used in describing granular flows.

pg. 4-11, line 6: Add "in part" before "because" as mechanisms other than mixing prevent particle deposition from being zero.

pg. 4-12, line 12: True, relatively few coarse particles will pass through the nose in an "average" person. However, some people have greater penetration, and even a few coarse particles can have appreciable masses.

Accordingly, I suggest adding a sentence at the end of this line, such as: "However some individuals have less efficient coarse particle deposition in the ET region, and such particles can carry significant mass into the tracheobronchial and alveolar airways."

pg. 4-13, line 1: Change "between" to "among".

pg. 4-15, lines 8 and 9: I don't know what "the maximum deposited incremental dose" is. Explain or delete the sentence.

pg. 4-18, line 9: Bennett and Zeman's "children" were age 7-14 years, so the result may not apply to young children. Insert "age 7-14 years" before "children". Infants and young children, e.g. age under 3-4 years, are very different than adults with respect to particle deposition. We must not assume that 7-14 year old children are representative of smaller children.

pg. 4-22, line 20: Change "humans" to "the average human", variability is significant in particle deposition. It is important that we recognize individual differences in dosimetry.

pg. 4-27, line 11: Change "Stat" to "that".

pg. 4-27, lines 29-31: Omit this sentence. Long-term TB retention of particles was discovered in rodents. The sentence may not be true in all cases.

pg. 4-28, line 6: Add "average" before "path length".

pg. 4-37, lines 6 to 7: Delete the sentence starting with "In contrast" as it is not always true.

pg. 4-44 to 51: Many journal titles are missing from the references.

Chapter 5

The chapter is thorough, but speculative, which is ok. The chapter does not address the importance of dose very well. This could be stated in the beginning of the chapter.

pg. 5-11, lines 1 and 3: Add "specific" before "larger", and add "the same mass of" before "particles of larger size".

pg. 5-18, line 12: Add "realistic" before "PM exposure".

pg. 5-32 to 5-39: Many journal titles are missing.

Poirot Comments (Mr. Rich Poirot)

July 2009 PM Integrated Science Assessment, Charge Question 6:

> *Several revisions were made to the evaluation of the welfare effects evidence in Chapter 9, in response to the CASAC PM Panel comment, to focus further on effects on climate and ecosystems and include further evaluation of urban visibility evidence, where possible. In addition, as recommended by the CASAC PM Panel, key findings and conclusions from this chapter were incorporated in Chapter 2. The discussion of PM effects on climate was increased with substantially more detail from recent publications, including discussion of specific climate forcing effects from individual PM components and size fractions. The discussion of ecological effects was also reorganized to focus on the types of effects and effects of individual components. For the effects of PM on visibility, new material was added including sections on direct optical measurements and the value of good visual air quality. Please comment on the effectiveness of the reorganization and revisions regarding welfare effects.*

Generally, the revisions made to Chapter 9 strengthen the chapter, improve its clarity and are directly responsive to previous CASAC comments on the 1st Draft ISA. A few minor revisions may be warranted, but I don't think any major revisions are required. The added discussion on direct optical measurement methods and on visibility valuation is helpful, although there is relatively little presentation or analysis of optical measurement data, and in particular, from measurements using combined nephelometer and aethalometer – equipped with various PM (1, 2.5, or 10 micron or "switching") size fractioning inlets. Presumably such measurements can be shown to agree reasonably well with transmissometers, aerosol reconstruction, etc. Better demonstration that there are currently viable, field-tested monitoring techniques to implement the proposed optical standard would be helpful in the ISA or should at least be added to the REA.

Substantial detail has been added on aerosol effects on climate, much of it taken directly from recent IPCC documents (which is fine – as these are current, relevant and authoritative). Unfortunately the quality of reproduced graphic images is extremely poor – although the fault is not with EPA, as the poor graphics appear to come directly from the original IPCC reports. While the introduction to section 9-3 indicates that the reproduced CCSP SAP2.3 incorporated "significant sections from EPA data and reports related particularly to U.S. emissions and measurements", there is very little reported in the chapter directly relating to emissions from or measurements within the US. While a number of causal relationships between emissions, aerosol concentrations and climate effects can be identified on global scales, there doesn't seem to be a clear, current basis for establishing specific US secondary PM standards for the purpose of ameliorating local or global climate effects. Consequently, I don't think it would be productive for staff to spend time adding to the aerosol/climate section in the current ISA.

In a similar way, the newly added details on ecological effects of various PM chemical components provides a much improved and more comprehensive summary of the subject area, but does not suggest that there's currently a strong justification for setting secondary PM standards to protect against adverse ecological effects at the present time, or for expending much additional effort on this section of the ISA in the current review cycle.

Specific Comments on PM ISA, Chapter 9:

p. 9-15, 2nd para, last sentence: Why not name the 5 urban areas with transmissometers? Also, this reminds me to suggest that if time allows, possibly the Phoenix hourly transmissometer data could be compared with the modeled hourly reconstructed aerosol extinction estimates – to help evaluate the quality of those estimates, and/or to suggest ways in which they might be improved.

p. 9-15, 3rd para, last sentence: A higher resolution (than what's routinely reported) version of the ASOS data is available (and more useful). EPA used to fund STI to routinely access and report this higher resolution data, but has discontinued support.

p. 9-49, 5th line from bottom: This very large (Title IV-related) drop in SO_2 emissions from 1994 to 1995 could be mentioned as a possible explanation for the apparent lack of post-1995 improvement in clean or hazy days at about half the Eastern IMPROVE sites in figs 9-26 & 9-27.

p. 9-88, Figure 9-50: The figure caption indicates the right figure includes effects from "nitrate" & OMC, while the Y-scale label and above the figure both indicate "Sulfate + OMC". Change "nitrate" to "sulfate" in the figure caption. It might also be noted that the RAIN network continuous sulfate data (as measured by Teco 5020) has been shown to be highly correlated with, but lower (by factor of 1.3) than collocated IMPROVE filter-based sulfate measurements. If the sulfate-associated extinction in left & right sides of Figure 9-50 were increased by 1.3 the slopes and R^2 would increase. This effect is shown in Figure 5.3 of the referenced NESCAUM report in which reconstructed B_{sp} from OMC + adjusted sulfate = 0.91 Measured B_{sp} + 4, R^2 = 0.94.

p. 9-95, 2nd para, last line: It would be useful here to also report other aspects (besides just the B_{ext} level) of the Denver standard – for example the fixed 8-hour 8 am to 4 pm daylight window, 4-hour averaging time and <70% RH constraints.

p. 9-96, 3rd para, last line: As for the Denver standard, why not report other aspects (besides just the B_{ext} level) of the Phoenix standard – the daylight window, 4-hour averaging time and <90% RH constraint. Also, the Phoenix "standard" is not based on an absolute threshold, but on a required improvement across the entire visibility distribution – moving bad days to moderate, moderate to good, good to excellent, etc. Discussing this might help emphasize that while there appear to be fairly convergent public opinions on levels of poor visibility that are considered "unacceptable" in the various studies, there are also adverse welfare effects from reductions in the frequencies of periods with moderate, good and excellent visibility, and would be benefits from improvements across the whole distribution. Conceivably this might lead toward considering a secondary "standard" which would be "progress-based" over fixed future time intervals, rather than "threshold-based" with an indeterminately-defined time fuse of "as expeditiously as practicable".

p. 9-98, last 4 lines: This observation that respondents were often "confused about the role of weather and humidity in the different visibility conditions presented in the photos" (even when a weather and RH-neutral WinHaze approach was employed) might also lead to a position that a good secondary NAAQS should be based on metrics that make as strong a distinction as possible

between effects of pollution and effects of humidity and other weather. Examples include: applying an RH filter (I think anything between the 70% used in Denver and 90% used in Phoenix could be justified); shortening the daylight window (to exclude the few most humid hours), increasing the averaging time (from 1 to 2, 3, or 4 daylight hours); and/or altering the form from the xth (90th, 95th or whatever) percentile of the worst 1 hr (or 4hr or 8 hr) in a day summed for the year to the xth (90th, 95th or whatever) percentile of the hourly (or 4hr or 8 hr) levels in a year or season. Any/all of the above will tend to "dry out" the metric, which would reduce differences between the West and the East, spatially and temporally focus regulatory efforts more on times and places of maximum pollution rather than maximum humidity, and provide the public with as clear a distinction as possible between effects of pollution and effects of humidity and other weather.

p. 9-102, lines 3-11: It might be helpful to include a complementary paragraph describing some of the disadvantages an optical measurement-only approach – especially as a basis for a standard. For example: cost and difficult siting criteria for transmissometers, similar cost and complex operational and data processing issues with nephelometers and aethalometers, absence of information on mass, size distribution or composition of pollutants causing the extinction. I think these measurement issues can be resolved, but it will require some effort from EPA and the states. It might be prudent to start with a small pilot network to find and work out some of the bugs.

p. 9-901, Figure 9-53, and elsewhere in this section: The quality of most of the graphic figures copied from the CCSP SAP2.3 is regrettably poor, although I note in checking the original reference its not your fault – the original is barely legible.

p. 9-131: You could add an example here on MODIS AOD vs. AIRNOW $PM_{2.5}$ from the EPA/NASA IDEA site that might be a clearer and more relevant illustration. http://www.star.nesdis.noaa.gov/smcd/spb/aq/index.php

p. 9-194, line 6: Its not clear what "to have a factor of 2" refers to.

p. 9-208-210: This section (9.3.9.3) is about the only place in section 9.3 that refers to any specific effects within the US or resulting directly from emissions from US sources (and which therefore might be relevant to consideration of secondary PM standards). Given this, it would seem important to be more clear about exactly what the PM causal mechanism(s) is (are). There are also indications that urban "heat islands" tend to increase convective precipitation in downwind areas (http://www.gsfc.nasa.gov/topstory/20020613urbanrain.html). See also the counter arguments presented by Alpert et al. (2008) http://www.tau.ac.il/~pinhas/papers/2008/Alpert_et_al_JAMC_2008.pdf Possibly there are also other non-aerosol effects of urbanization, such as more rapid runoff and deforestation, that would tend to alter downwind precipitation patterns.

p. 9-210, lines 17-18: This description of "planet brightening when seen from space because aerosols scatter most of the visible spectrum light" isn't quite right. Most aerosol-scattered light is ultimately scattered in a forward direction. The "brightening" results only from that (relatively

small, 10-15%) fraction of visible light that is back-scattered in the direction of the hypothetical observer in space.

p. 9-211, 2nd para, line 1: Not clear what you mean by "progress has been made with in-situ and remotely sensed aerosols."

Russell Comments (Dr. Armistead (Ted) Russell)

First, I note that the word concise was removed from the first sentence, as is appropriate. When I showed my air pollution physics and chemistry students the PM ISA, they said "Can't they shorten it?", to which I replied this is shortened from the old Criteria Document approach, and it should demonstrate how active is the field. (I also noted to them how much more is known now then when I took the course about 29 years ago when taking a one semester course pretty much put you near the front of the field.) On that note, however, I do think that future versions (in coming years, not in the revision to this one) should be shortened. I found each section to be extremely thorough and providing more information than needed to adequately inform the process. This was particularly true for Chapter 3 (and this view may be due, in part, to being most familiar with that area), where a part of the material will likely not have much role in further review of the NAAQS. It almost appeared as though it was reverting back to the old AQCD approach.

In spite of the call to shorten future versions, overall, I think the ISA has been improved significantly. I still view that it does not bring enough attention to compositional differences in PM effects (both health and welfare). There is significant information that carbonaceous aerosols (typically referred to elemental and organic carbon) are of greater concern for many endpoints. The ISA should lay out this information more completely.

I continue to worry about the treatment of climate. While the inclusion of parts of the CCSP provides the foundation for discussing PM impacts on climate, given the importance of this issue, and how it could impact how a secondary NAAQS might be formulated, a bit more analysis would have been beneficial. Composition and size is very critical here, but is not fully transmitted in the synthesis chapter.

Chapter 2 does a reasonably good job of integrating the findings of the rest of the ISA, though a few improvements can be made. The major concern I have, at present, echoes the comment above that there is not enough emphasis on compositional differences and their implications. I would add to the Section 2.4," Policy Relevant Considerations" (or possibly a new section "2.6. Composition Considerations" since it synthesizes beyond just health effects),a subsection on composition that integrates what we understand and suspect about compositional differences on health and welfare effects. A particular finding in such a synthesis could be that control of organic and elemental carbon (EC/OC) PM from sources such as automobiles and biomass burning appears to be more beneficial than controlling other components of PM (or it could be couched that a EC/OC has greater deleterious impacts than the same amount of other components).

I think in prior ISA's, there was a summary table of those impacts that were causal, likely to be causal and suggestive right at the start of the section on effects. This should be followed here. It is a bit odd that you find out the "inadequate" relationships first. Thus, add a summary table at the beginning of 2.3 of the health effects examined. I find it a bit unnatural to suggest that the evidence for the relationship between PM and visibility to be "strong and consistent" in that it is well beyond strong and consistent, and if this were not the case it would be in direct contradiction to our basic understanding of physics. While such terminology is appropriate for the health effects where such a direct linkage is not so established, here it just seems odd.

A final synthesis section might be useful that puts it all together, saying that PM with certain characteristics/sources has the following impacts on what aspects of BOTH health and welfare (and strength of association). This section would also synthesize uncertainties as to how they impact our overall understanding and how to interpret results.. At present the chapter does not really synthesize health and welfare and how the various uncertainties impact our overall understanding, and ends rather weakly. Might there be a section synthesizing uncertainties (possibly in the section discussed above or separately?

Minor:
2-7-28: should be ."…oxidation of isoprene, terpenes and…"
2-8-1 This is still in the research phase and its importance is still being explored.
2-9-28: Explain the variation in PRB levels.
2-9-33: Weak beginning of a section.2-11-28/30: I would hesitate to state this as such as it may impact the use of such information in other assessments and it is not apparent you are using this information in this assessment.
2-14-10: Font on $PM_{2.5}$
2-14-14: You might provide a bit of explanation as to why this is consistent with other null findings in the West.
2-19-12 (and related section in the report). In the section above, it appears as though the information for this endpoint is very similar to that for acute CVD where the relationship was found to be causal. Why the difference?
2-25-14/29 Much of what this section appears to be trying to explain can be explained by compositional/source differences as opposed to the items discussed here, and I think compositional differences provide a better explanation.
Section 2.3.5: It should be noted that UFP effects can not be separated from compositional effects. Indeed, there are results that might suggest that sulfate-dominated UFP do not have the same effects seen for CAPS and DE.
2-34-29: Status is not protective… I would say nutritional status can affect response.
Section 2.4.2: Lag structure is not so important here as the other two, and these parts could be integrated in to the appropriate sections discussing the specific health endpoints.. It may be important to interpreting the epi studies, and how they were conducted, but as presented this section does not have that much to say as to whether the causal/likely causal… decisions were appropriate, nor guide what the level of the standard might be chosen to be. For this section to stand alone, here, the discussion of lag structure between the endpoints needs to be synthesized.

Chapter 3
As noted above, this chapter is very thorough, and is likely more exhaustive than necessary. I still might have provided a bit more on the evaluation of exposure models, but if that is done as part of the Risk Assessment, that is fine. In general, I found it to be balanced and correct, with a few exceptions.

As an example of where the chapter really goes in to unnecessary detail, and where this leads to an error, on page 150, they note that three dimensional CTMs typically use finite difference or finite element approaches. This level of detail is not overly informative to reviewing the NAAQS. Further, many models use finite volume approaches. Further, the approach used for

deposition is incorrect for particulate deposition (there is no sedimentation velocity in the formulation given), and the whole discussion of deposition could be shortened.
I was a bit taken aback by the paragraph on page 3-225 saying "Clearly there are variations…", concluding that ""too poorly characterized on a broad scale to allow conclusions to be drawn…" I thought NARSTO did just that. While there are variations, there are typically consistent features as well. This paragraph strikes me as a bit negative.

The last paragraph on page 3-226 seems out of place, since it is talking about impacts on the health effects studies discussed later, and I did not pick this up from the chapter (I may have missed it).

Minor:
Figure Numbering: It appears as though figures were removed, leading to figure numbers later in the document being off.
3-13-22: You need to be very careful in how you interpret AMS measurements in terms of what is secondary or not. They measure spectra and hypothesize what fraction is secondary.
3-15-8: The 2.8% contribution to OC is a bit misleading in that it represents only the two diastereomisomers, and more SOA from isoprene can be present.
3-18-15: Should just be Maricq. (also line 20)
3-21-6: (eqn 3-1) This is not truly correct, particularly for particles, and wet deposition is usually parameterized differently as well. This section is probably longer than needed here in that what is of importance is to note the typical lifetimes and loss processes.
3-33-21: What is meant by reliable, noting that the prior discussion also suggests it is consistently impacted by artifacts?
3-34-5: nonvolatile.
3-37-25: "AMS RESULTS did not…"
3-82-4: Move "only" about 5 words down.
3-82-21: I would remove "slightly".
3-83-5 "…where atmospheric nucleation"
Figs. 3-42/43: Usually the sizes are given small-big.
3-186: I would be a bit more tentative about deriving $PM_{10-2.5}$ from the $PM_{2.5}$ and PM_{10} values. It is almost assuredly true that there is some correlation in the PRB PM_{10} and $PM_{2.5}$ values calculated by Trijonis, and the current approach would actually indicate that in some circumstances, $PM_{10-2.5}$ is ~90% of the PM_{10}, which is almost assuredly not true. Use typical $PM_{2.5}/PM_{10}$ ratios for the two regions to get a better estimate of the range in the values.
Tables 3-19-23…: In many cases, the micro sign is given as a box.

It is sometimes the case that the rest of the sentence after an equation is given is indented (e.g., 3-205-14).
3-223-18: "higher in clear"
3-223-19: remove the ";"
3-224-3: Use ~34 times more
3-225-25: "… 1-h commute…'

Speizer Comments (Dr. Frank Speizer)

Chapter 2

General Comments:

EPA Staff are to be commended for doing an excellent job in pulling together and presenting in a very readable format the summary of the data contained in the ISA. By placing the conclusions here with appropriate documentation of where to find the primary discussed data, the whole document becomes more useful.

Specific Comments:
Page 2.5, lines 14-19. Although accurate as stated, what seems to be left out in the comparison of $PM_{2.5}$ to PM_{10} is that the PM_{10} correlations in themselves (.70) are really remarkably high and suggest, although not quite as consistent as $PM_{2.5}$ that they can be usefully used to model exposure. It might be worth mentioning this.

Pge 2.6, line 30. Isn't there also the potential for greater production in the winter of NO2 (though less efficient winter burning or greater production) to lead to increased quenching of O3?

Page 2.13, lines 21-25 bullets. It might be useful to add to the end of each of these lines the specific sections in Chapter 6 or 7 where each topic is discussed. Although I can agree with each of the conclusions, I can imagine some "stakeholders" wanting to raise questions and getting hung up on not having the specific background data to support the statement. By providing the specific paragraph reference it would make documentation easier.

Page 2.14, Table 2.1. This may be quibbling over semantics. I like putting the summary table up front. However, by describing the effects as indicated, the suggestion is that short term exposure is causing a chronic condition. These effects are for the most part acute events occurring among persons with chronic conditions. (If the table occurred after the descriptions that follow there would be no problem). Perhaps a modest change in the Table title or a footnote would help.

Page 2.15, first two paragraphs. I would suggest reversing the order of these paragraph (with minor editorial changes). Offering the fresh diesel exhaust data before the $PM_{2.5}$ data seems to be mixing the consistency argument by suggesting that UFP are explaining $PM_{2.5}$ effect when they are really supplementing the findings of the $PM_{2.5}$ effects reported in the second paragraph.

Page 2.21 and 2.22, Figures 2.1 and 2.2. Ordering the points in these figures by level of exposure estimate has made them less useful. They mix up outcomes that really cannot be looked at as a result of gradient of exposure. It would be better if they were divided into small figures by specific outcomes, and then look at gradients of exposure.

Pages 2.26l-2.30, whole section. Not enough emphasis is made of the fact that for each of the outcomes discussed there are only a limited number of studies, thus the designation of

suggestive. Again breaking out the kinds of outcomes in Figure 2.3 would be better than lumping them all together.

Page 2.29, Figure 2.3: There is clearly something wrong here. The units in this Figure are wildly different from Figure 2.1 and 2.2, and are simply not believeable. I just may be a labeling problem, but it needs to be fixed.

Page 2.33, paragraph beginning on line 14. Some editing needed. The first sentence says controlled study effects seen in susceptible subjects with CVD and/or respiratory diseases the last sentence says respiratory diseases. Suggest change the last to cardiorespiratory diseases.

Responses to Charge Questions ***(paraphrased and shown in italics)*** on ISA Draft 2

1. Evaluation of health evidence in Chapters 6 and 7
   a. ***The role of the studies of PM_{10} in consideration in causality determinations for $PM_{2.5}$ and $PM_{10-2.5}$.***

      Although this seems perfectly appropriate, it would seem that leading into this argument there should be some material (which I looked for in Chapter 3, but could not find, maybe just my inability to find) that could be referenced here or perhaps even summarized to justify the correlative nature of the relationships. This would help justify using the PM_{10} studies when neither $PM_{2.5}$ or $PM_{10-2.5}$ were available to further assure the consistency of the data.

   b. ***The inclusion of cause-specific mortality as part of suite of CVD and respiratory effects, in the development of causality judgments.***

      The use of cause-specific mortality provides a refinement of the data that is logical and appropriate. Since the bulk of the mortality is dominated by cardiovascular deaths it is appropriate to show these separately, and similarly since respiratory deaths are the fourth leading cause of deaths these also provide important information. By showing these two classes of death separately and then showing the total (which is clearly dominated by these two, but less subject to reporting or disease classification error) the reader gets a better understanding of both the magnitude and nature of the deaths that are occurring.

   c. ***Scope of evidence considered in the causality determination for ultrafine PM.***

      The change of the designation from inadequate to suggestive appears to be dominated by the interpretation of the relatively greater number of clinical and toxicological studies of diesel and gasoline exhaust studies, that are clearly dominated by UFP. This is in contrast to the few epidemiological studies, that are for the most part null or poorly defined as UFP exposure studies. Thus, the designation of suggestive is rational and probably right, but clearly the designation itself will need additional work in the future to either sustain or refute the designation. This probably should be indicated.

Charge Question 1d:

   d. ***With regard to the role of PM in mutagenicity, genotoxicity and carcinogenicity comment upon the expansion of this evaluation to include a summary of toxicological studies using routes of exposure other than inhalation, as well as consideration of both mortality and incidence studies.***

Staff has done an excellent job in summarizing a complex literature related to both the general and specific associations of using mutagenicity, genotoxicity and carcinogenicity studies in assessing the PM effects on cancer. The charge question is really in two parts. With regard to using routes of exposure other than inhalation, to assess mutagenicity and genotoxicity, these are standard procedures used in the field and have formed the basis of much of the general literature basis of mechanistic understanding in mammalian cancer research. There are examples where such studies have resulted in leads to where to look for cancer risks in humans. Thus it is appropriate to use such data in determining where along the spectrum of certainty with regard to causality these studies should be considered. Secondly, with regard to the population studies that are reported in the last few years, these have been large, well assessed groups, in which the same exposure parameters have been used for cardiovascular and respiratory findings (that appear to be defined as causal associations) with an outcome that is well defined, albeit it dominated by the potential confounder of smoking. The relatively consistent finding of lung cancer excesses as an exclusively associated cancer, along with the attempts to control for smoking are suggestive, and thus the appropriate interpretation and designation appears to have been made.

2. Revisions to Chapters 1, 4, 5.

Chapter 1, expansion or additions to sections on history of previous PM NAAQS reviews.

It seems to me this is just about right. There is a slight shift of tone from the early historical discussion of setting the NAAQS to a more "legalistic" description of what has gone on in the last 10 years or so. I found one issue (described in a separate memo) with regard to table 1.2 on page 1.26. The category of Experimental Evidence seems inappropriately defined.

Chapter 4, and 5 I leave to others to comment upon.

3. Chapter 8 Susceptible populations

Please comment on the organization and presentation in Chapter 8 of evidence regarding susceptible subpopulations

Although the Chapter summarizes definitions used by others (and EPA) for susceptibility, the definitions provided are not very useful. It might have been better to talk about host vs environment more formally. In addition, in discussing each of the "susceptibility factors" much of what is reported is really not much different that what is contained in Chapters 6 & 7. However, the discussion is better organized in defining and using susceptibility factors as related to PM exposure. What is clearly left out, and perhaps should have a brief discussion is a contrast between susceptibility and vulnerability and how these factors play into a discussion of risk and margin of safety.

4. Chapter 3.

Comments on revisions

This chapter read rather well. I leave to others specific comments on Sections 3.4 and 3.5. In section 3.8 the Staff has reviewed the factors potentially influencing exposure levels for health studies. I would suggest a summary table at the end of this chapter that takes all the factors and provides qualitative directionality for the potential factor in biasing away or toward the null (or not at all). This I think would identify more readily for the reader what to worry about and what not to be concerned about.

5. Chapter 2.

Please comment on the integration.

I believe this is an important chapter and I have already submitted comments on this chapter separately. I repeat them here simply to put all my comments together. Clearly I have done this in greater detail than what I have done to answer other questions.

Suh Comments (Dr. Helen Suh)
Charge Question 3:

Revisions to Chapter 3 on Source to Exposure: Consistent with revisions made to the health effects chapters, Chapter 3 was revised to clarify that PM10 incorporates both PM2.5 and PM10-2.5 and reorganized to begin with PM2.5 and PM10-2.5, followed by PM10, where applicable. The discussion of measurement techniques and chemistry of PM10-2.5 has been expanded in Sections 3.4 and 3.5, in response to CASAC comments. In addition, Section 3.8 on human exposure to PM has been reorganized and expanded to better characterize the evidence and provide useful information for interpretation of epidemiologic studies. We would appreciate comments from the CASAC PM Panel on these revisions.

The Chapter is a massive and comprehensive summary of the current state of the PM sources, monitoring and modeling methods, concentrations and exposures. The Chapter was generally clear, comprehensive, and well organized, which is notable given the amount of information it contains. It clearly and appropriately incorporates comments from the April review. Of note, the relation among $PM_{2.5}$, $PM_{10\text{-}2.5}$, and PM_{10} was greatly clarified and the inclusion of additional information on UFP, PM components, and $PM_{10\text{-}2.5}$ monitoring methods was welcomed. Similarly, the organization and content of the exposure section was greatly improved, especially with regards to the relevance of exposure findings to epidemiologic studies. While significantly improved, further improvements could be made to the exposure section to help with the organization, seeming overlap with earlier sections, and clarity, as discussed briefly below.

- Given the importance of measured PM in the earlier sections of the Chapter, in the epidemiological studies, and also in the Health REA, it makes sense to place the discussion of exposure measurements before that for exposure modeling. Further, the exposure measurements section should include discussion of new methods that have been made to measure (1) personal exposures to total PM, (2) PM of outdoor origin, (2) outdoor concentrations outside individuals' homes, and (3) indoor PM exposures to total PM and to PM of outdoor origin). In this context, studies using tracers of outdoor or regional pollution can be introduced.
- The discussion of each topic should be consolidated into single sections, with references to this section made as necessary in later sections. As is currently written, certain topics, such as spatial variability and particle infiltration, appear repeatedly in several subsections. The discussion on these topics would be more focused and less confusing if their discussions were consolidated.
- In Section 3.8.4.3, it would be helpful to clarify which component of PM is being discussed. Further, within each subtopic or heading, separate or otherwise distinct discussions for $PM_{2.5}$, $PM_{10\text{-}2.5}$ and the PM components would help with clarity.
- Section 3.8.4 (Exposure Assessment Studies at Different Spatial Scales) and its subheadings are misnamed. While the heading titles do provide parallels with earlier sections of Chapter 3, they do not accurately describe their contents. For example, the section 3.8.4.1 does not actually discuss urban scale ambient PM exposure, rather issues related to exposure error, exposure modeling, and tracers of ambient particles.
- It would be helpful to include a subsection in the beginning of the section, perhaps in Section 3.8.1 (General Exposure Concepts) that summarize the range of measured exposures to

$PM_{2.5}$, $PM_{10-2.5}$, and PM_{10}, their composition, and differences by city, susceptible group, and season.

- Section 3.8.6: Other factors that could affect exposures are worth noting, such as home ventilation patterns and activity patterns.
-

Response to Charge Question 4

Charge Question 4:

Revisions to Chapter 3 on Source to Exposure: Consistent with revisions made to the health effects chapters, Chapter 3 was revised to clarify that PM10 incorporates both PM2.5 and PM10-2.5 and reorganized to begin with PM2.5 and PM10-2.5, followed by PM10, where applicable. The discussion of measurement techniques and chemistry of PM10-2.5 has been expanded in Sections 3.4 and 3.5, in response to CASAC comments. In addition, Section 3.8 on human exposure to PM has been reorganized and expanded to better characterize the evidence and provide useful information for interpretation of epidemiologic studies. We would appreciate comments from the CASAC PM Panel on these revisions.

The Chapter is a comprehensive summary of the current state of the PM sources, ambient aerosols, monitoring and modeling methods, concentrations and exposures. The Chapter generally reflects the state of science in a clear, comprehensive, and well organized fashion, which is notable given the amount of information the Chapter contains. Further, the Chapter revision appropriately incorporates comments from the April review. Of note, the relation among $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} was greatly clarified and the inclusion of additional information on UFP PM components, and $PM_{10-2.5}$ monitoring methods was welcomed. Similarly, the organization and content of the exposure section was greatly improved, especially with regards to the relevance of exposure findings to epidemiologic studies. While significantly improved, further improvements could be made to the exposure section to help with the organization, seeming overlap with earlier sections, and clarity, as discussed briefly below.

Specific comments:

- Standard Reference Materials (page 2-20, line 20): It says "To date, there are few standard reference materials ..."
  This sentence should be reworded to make it clear that we currently do not have a way to assess mass concentration measurement accuracy, as there are no materials (to our knowledge) that provide a test of accuracy or airborne PM mass. There are, however, SRMs that are useful for testing the accuracy of the analytical methods for PM composition.

- Policy Relevant Background (PRB)
  There are the usual concerns regarding the policy relevant background (PRB). The EPA has to set a health-based standard irrespective of the background concentration of particles and thus, the PRB is really an implementation issue and not a regulation setting issue. As the PRB increases because of activity outside of the United States, there is decreasing flexibility in attaining concentrations that are fully protective of public health. The modeling approach has some appeal, but given the problems with the accuracy of the emissions inventories in the US where substantial effort and resources are expended to develop them and there are still problems, the likelihood that we can adequate model emissions in the rest of the world seems very low. It would seem that there could be some comparisons between the model-based

approach and the remote site approach to provide some basis for confidence in the model estimation of the PRB.

- Exposure Section
  - Given the importance of measured PM in the earlier sections of the Chapter, in the epidemiological studies, and also in the Health REA, it makes sense to place the discussion of exposure measurements before that for exposure modeling. Further, the exposure measurements section should include discussion of new methods that have been made to measure (1) personal exposures to total PM, (2) PM of outdoor origin, (2) outdoor concentrations outside individuals' homes, and (3) indoor PM exposures to total PM and to PM of outdoor origin). In this context, studies using tracers of outdoor or regional pollution can be introduced.
  - The discussion of each topic should be consolidated into single sections, with references to this section made as necessary in later sections. As is currently written, certain topics, such as spatial variability and particle infiltration, appear repeatedly in several subsections. The discussion on these topics would be more focused and less confusing if their discussions were consolidated.
  - In Section 3.8.4.3, it would be helpful to clarify which component of PM is being discussed. Further, within each subtopic or heading, separate or otherwise distinct discussions for $PM_{2.5}$, $PM_{10-2.5}$ and the PM components would help with clarity.
  - Section 3.8.4 (Exposure Assessment Studies at Different Spatial Scales) and its subheadings are misnamed. While the heading titles do provide parallels with earlier sections of Chapter 3, they do not accurately describe their contents. For example, the section 3.8.4.1 does not actually discuss urban scale ambient PM exposure, rather issues related to exposure error, exposure modeling, and tracers of ambient particles.
  - It would be helpful to include a subsection in the beginning of the section, perhaps in Section 3.8.1 (General Exposure Concepts) that summarize the range of measured exposures to $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10}, their composition, and differences by city, susceptible group, and season.
  - Section 3.8.6: Other factors that could affect exposures are worth noting, such as home ventilation patterns and activity patterns.

Vedal Comments (Dr. Sverre Vedal)
1a. Use of PM_{10}.

Findings pertaining to PM_{10} in this 2nd draft are discussed in conjunction with two component fractions ($PM_{10-2.5}$ and $PM_{2.5}$); causal determinations are no longer provided for PM_{10} itself. There is value in this approach, since both fractions comprise PM_{10}. It does not, however, seem logical that evidence on PM_{10} would be equally relevant to both $PM_{2.5}$ and $PM_{10-2.5}$. In some regions of the country PM_{10} is more reflective of $PM_{2.5}$ whereas elsewhere PM_{10} is more reflective of $PM_{10-2.5}$.

In the respective PM fraction Summary and Causal Determinations sections, there is little mention of PM_{10}. Where PM_{10} is mentioned in this context, it only comes up in support of $PM_{2.5}$ (e.g., PM_{10} evidence is cited as strengthening the evidence for $PM_{2.5}$-related respiratory effects [p. 6-244] and for mortality effects [p. 6-317]). PM_{10} evidence is not used in specific support of $PM_{10-2.5}$ effects. Yet in the discussion of short-term PM exposure mortality effects (section 6.5.2), PM_{10} studies are cited as providing "an underlying basis for the overall pattern of associations observed when examining the relationship between $PM_{10-2.5}$ and $PM_{2.5}$ and mortality." There is inconsistency then in the way PM_{10} findings are used.

PM_{10} findings are also used in evaluation of long-term PM fraction exposure effects (e.g., p. 7-24). For respiratory morbidity effects of long-term PM exposure, a more precise argument is made that "studies showing associations only with PM_{10} were conducted in locations where PM was predominantly fine particles, providing support for associations with long-term exposure to fine particles" (p. 7-28, line 32; p. 7-60, line 16). However, in some studies effects are only seen for PM_{10} and not for $PM_{2.5}$ (p. 7-43, line 6), which is not consistent with that statement.

In order to better interpret PM_{10} findings relative to those of $PM_{2.5}$ and $PM_{10-2.5}$, it would have been helpful, perhaps in Chapter 3, to include and/or highlight data on the relationship between PM_{10} and both $PM_{2.5}$ and $PM_{10-2.5}$, stratified by region of the country. Also, in light of the role of the current 24-hour PM_{10} standard with respect to $PM_{10-2.5}$, it would be important to bring together the evidence relating to PM_{10} that allows it to be used for this purpose.

In short, the way in which PM_{10} is used is vague and inconsistent. PM_{10} evidence is used generally to support overall effects of PM, but specifically only in support of $PM_{2.5}$ effects. The role of the current PM_{10} standard, however, is in controlling $PM_{10-2.5}$. Better justification for the utility of PM_{10} findings is needed from a scientific and policy perspective. Nevertheless, providing causality judgments for $PM_{10-2.5}$ and $PM_{2.5}$, but not for PM_{10}, as is done in the current draft, is more in line with the current science.