UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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EPA-SAB-CASAC-LTR-01-001

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

Honorable Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Review of the *Air Quality Criteria Document for Particulate Matter: Second External Review Draft* (EPA 600/P-99/002bB): A CASAC Review

Dear Governor Whitman:

The Clean Air Scientific Advisory Committee (CASAC) of EPA's Science Advisory Board, supplemented by expert consultants (together referred to as the "Panel"), met on July 23-24, 2001 to review the March 2001 draft document, *Air Quality Criteria for Particulate Matter - Second External Review Draft* (EPA 600/P-99/002bB) (EPA, 2001), in a public meeting in Research Triangle Park, NC. This was the second CASAC review of the draft Criteria Document (CD) for particulate matter (PM) in the current cycle for reviewing the National Ambient Air Quality Standards (NAAQS) for PM. CASAC review of this document is required by section 109 of the Clean Air Act.

As noted below, the CASAC could not come to closure on this draft document and has requested that the Agency revise the draft for another review.

1. BACKGROUND

The Panel reviewed the First External Review Draft of the PM Criteria Document (EPA, 1999) in December 1999, focusing primarily on the organization, structure, and presentation of material in the draft document. It was understood that this was an early incomplete draft and that additional information would be incorporated in subsequent drafts. There was no intent nor expectation that the Panel would close on the draft document at this stage of its development. The Panel was generally complimentary about the content and quality of this draft, while noting the need for considerable development both in structure and content (CASAC, 2000).

The EPA has assessed approximately 1800 new references published since the October 1999 First External Review Draft (EPA, 1999) was released for CASAC review. This assessment, along with responses to CASAC's earlier comments (CASAC, 2000), are incorporated into the Second External Review Draft.

2. REVIEW OF THE APRIL 2001 SECOND EXTERNAL REVIEW DRAFT CRITERIA DOCUMENT FOR PM

The Panel was impressed with the revised version of the Draft Criteria Document as compared to the version that was reviewed in December 1999 (EPA, 1999). It is clear that the comments provided by the Panel on the prior draft were seriously considered and efforts made to address the issues and concerns that were raised. A large body of new literature has been published in the intervening time and the staff has clearly made a substantial effort to incorporate as much of it as appropriate. The Panel felt that this version represented a significant step toward achieving an acceptable summary of the available science. The Panel was unanimous in its view that the document was not yet ready for closure, but it was our opinion that appropriate modifications to the present document should permit closure.

In this report, we summarize the major questions, concerns, and issues that were expressed regarding the Draft Criteria Document. There were extensive comments from the members of the CASAC PM Panel and they are provided in appendices to this report. These comments are considered an integral part of this report, and the Agency is encouraged to take them into consideration in making further revisions to the document.

2.1 Major Issues

A major global concern of the Panel was the lack of adequate linkage among the chapters so that the Document presents a consistent and coherent summary of the science. We suggest that the chapters could be realigned using the paradigm presented by the National Research Council Committee on Research Priorities for Airborne Particulate Matter (NAS, 1999). The paradigm begins with emissions from sources and follows the path to concentrations, exposure, dose, and effects. We suggest moving the dosimetry chapter (Chapter 7) to precede the epidemiology chapter (Chapter 6) and it should be linked to exposure as described in Chapter 5. This framework could also serve as a basis for organizing the synthesis chapter (Chapter 9). There are other possible unifying themes that could be used, and we suggest that using such an approach would provide more coherent flow to the document. The approach should be described in Chapter 1 and would provide a clearer path through the wealth of new information that needs to be reviewed and synthesized into a picture of our current state of knowledge.

A second major concern was the limited information on coarse thoracic particles ($PM_{10-2.5}$) in many of the chapters. The Court of Appeals (1999) decision in American Trucking Associations vs. EPA precludes having both PM_{10} and $PM_{2.5}$ standards. Thus, it is critical that the document clearly defines the information that is and is not available on $PM_{(10-2.5)}$. There is a clear distinction made between the roles of $PM_{2.5}$ and $PM_{(10-2.5)}$ in Chapters 4 and 6. However, Chapters 2, 3 and 5 do not adequately distinguish the measurement methods, ambient concentrations and distributions, and exposure issues associated with the two size ranges. There is also no discussion of the toxicology of thoracic coarse particles in Chapter 8. Although extensive information may not be available, it is critical that the document clearly describes what scientific information is and is not known about $PM_{(10-2.5)}$.

A third major issue is the need for more emphasis on the new information concerning better time resolution in measurements. Our understanding of the atmospheric processes, exposure, and epidemiology is currently limited by the fact that most data represent integrated 24-hour samples. One of the major differences between PM and the gaseous criteria pollutants is the greater difficulty in making hourly or even shorter interval measurements. Such data allow the evaluation of effects at various integrating times. Such evaluations are currently not possible because of the limited amount of shorter sampling interval data.

However, major improvements in semi-continuous measurement methods for PM are now beginning to provide one-hour or better time resolution. The evaluation of these instruments is a major focus of several of the current Supersite activities. There have been publications showing extremely high short-term excursions in the PM concentrations. For example, Michaels (1996) does discuss some of the developments in measurement methods, but there is not an explicit discussion of such data in the exposure or epidemiology chapters (current Chapters 5 and 6). There have been a limited number of epidemiological studies based on short term data which were not explicitly evaluated (e.g., Morgan et al., 1998; Simpson et al., 1997). Thus, there is a developing information base that could be used in the future to reexamine the averaging time interval for the short-term PM NAAQS. It would be useful for this version of the PM Criteria Document to more explicitly recognize this direction. For example, it would be useful to have a subsection in Chapter 6 discussing the limited epidemiological studies that have been made with short interval data with a parallel section in Chapter 5 evaluating the complementary exposure information.

The document provides a detailed description of our current knowledge, but does not fully discuss its limitations. For example, the focus of epidemiological studies has been 24-hour integrated, PM_{10} mass since there is a large available data base. Additional studies have made use of the data that have been collected, but there cannot be extensive studies of specific chemical constituents, different integrating times, etc., because the data do not exist. A broader discussion of the limitations of our current state of knowledge particularly in the context of the extensive ongoing research and monitoring programs that EPA is supporting would be helpful in providing a better perspective on the current status of our knowledge of PM and its effects.

2.2 Chapter Issues

With respect to individual chapters, the specific Panel member comments provide considerable guidance for the needed changes (see Appendix A). There were no major structural issues with Chapters 2 and 3 other than the general framework question raised above. However, Chapter 3 must include a stronger discussion on the emission of precursors and formation of Secondary Organic Aerosol (SOA). At present, the emissions section almost exclusively discusses primary particles, which do not represent most of the fine particle mass in many locations. These chapters help to provide the background to the exposure and effects chapters and need to reflect that direction.

Chapter 4 (Environmental Effects of Particulate Matter) was a substantial improvement from the chapter on welfare effects in the earlier version of the CD. One important issue that is not currently included in the chapter was the potential for effects of PM on urban vegetation.

The chapter would be improved if the ecosystem and other welfare effects presentations were more focused on information that addresses key questions in the setting of standards, linking exposure to effects. Currently, the document addresses putative effects without an adequate discussion of what PM exposure and deposition are in the environment. Such a setting would make it clearer as to purpose of the chapter and would also link the chapter on the environment to the chapter on exposure. Finally, the purpose of the current economics discussion is unclear. It needs to be either better focused or potentially eliminated.

In Chapter 5 (Human Exposure to Particulate Matter and its Constituents), a clearer discussion of the chapter goals within the overall framework of the document would be helpful in evaluating the information being presented. The processes that lead to exposure are non-linear in nature, but the chapter appears to suggest that they are linear. There needs to be more emphasis on distributions of exposure as well as point estimates of the average exposure. It also needs to provide a better description of exposure error so that it provides the background for the discussions of exposure error problems in the epidemiology chapter. It needs to better reflect the complexity of the relationships between ambient concentrations and personal exposure. The chapter also needs to provide the background on the data needed to estimate dose, and particularly dose to target organs like the heart.

One of the major areas of the discussion was the epidemiology presented in Chapter 6 (Epidemiology of Human Health Effects from Ambient Particulate Matter). We recognize the problem of summarizing such a large body of work and then presenting and evaluating a limited number of specific studies that are most relevant to the understanding of the relationships between exposure to PM and health effects. It would be useful to establish a well defined set of criteria for choosing studies selected for detailed discussion. A clear description of the selection criteria needs to be added to the chapter. There also needs to be a uniform strategy for evaluating the studies that are discussed and for making comparisons among studies. We recognize that it is important for there to be careful evaluation of the major new studies. However, without well defined criteria for evaluating the studies, the presentation and evaluation of the studies and their results may not be uniform. It is also important to be very careful in the definition and consistent use of terms. Concepts such as “confounding” and “modifying” especially need to be defined and used consistently.

We suggest that additional summary tables be provided that present the key features of the studies and their findings. It may be useful to move the current detailed tables to appendices to the chapter and utilize the summary tables in the text.

One of key findings of recent large studies (Samet et al., 2000a; Samet et al., 2000b) is that there is heterogeneity in the relationships between PM_{10} and health outcomes among a number of locations. There are several possible explanations for this observation and these possibilities need to be presented. Is the apparent heterogeneity a random effect or is there real systematic variation in PM_{10} toxicity from location to location? Do multiple populations need to be considered separately, such as those living in air conditioned vs. non-air conditioned buildings? Are there differences among locations because of differences in the relative sizes of these multiple populations? Although the underlying cause of the heterogeneity is not yet

known, the potential causes deserve more discussion with regard to their implications for estimating exposure/response relationships.

The chapter currently contains little discussion of what is known regarding the relationship between PM exposure and cancer. Given the extensive discussion of this topic with respect to diesel exhaust particles and the ubiquitous presence of diesel as a component of the ambient aerosol, this issue should not be ignored in the Criteria Document.

Finally, discussion of epidemiology studies on morbidity/mortality effects on the fetus, neonates and infants should be expanded to better reflect the current state of knowledge.

Chapter 7 (Dosimetry of Particulate Matter) provides an extensive discussion of dosimetric models, but was no effort to use this knowledge to connect information on exposure, dose, and health effects suggested by toxicology or epidemiology. The connections could be greatly improved by moving this chapter to follow the exposure chapter, by including illustrative examples of relationships between particle size and regional deposition, and by providing examples of the magnitude of deposited and retained doses resulting from environmental exposures. This information is critical to setting the stage for evaluating how toxicological information might apply to the epidemiological observations in subsequent chapters.

Chapter 8 (Toxicology of Particulate Matter) is very selective in the choice of toxicological studies presented. Again a clearly defined set of criteria for choosing studies is needed as well as a discussion of how the toxicology helps to provide understanding of the relationships observed in the epidemiological studies. The relationship of this chapter with the rest of the document needs to be better defined.

The chapter should not only review key recent findings and advances since the last Criteria Document, but it also needs to discuss how the toxicology results help our understanding of the exposure-dose-response relationships observed in the epidemiological studies. An important facet of the discussion should be the relationship between doses used in the different toxicological approaches and doses received by people from environmental exposures. With these modifications, the value of the chapter within the context of the entire document will be greatly enhanced.

As indicated previously, the chapter needs to point out data which help our understanding of the toxicology of thoracic $PM_{(10-2.5)}$. It is not clear how much of such information exists, but to the extent it is available, it needs to be presented and the limitations of our knowledge of $PM_{(10-2.5)}$

It is especially important that the toxicological studies using concentrated ambient particles (CAP) be discussed thoroughly. Such studies are potentially very valuable; however, the CAP studies differ from studies of laboratory-generated atmospheres in that the cells and animals are not exposed to material that can be predicted in advance and reproduced as desired. Because the composition of CAP varies in both time and location, a thorough physical-chemical characterization is necessary to compare results among studies or among exposures within

studies, or to link particle composition to effect. The chapter should portray this issue and note that while studies incorporating sufficient characterization have high value, those lacking characterization have minimal value. Care also needs to be taken in discussing studies of ultrafine particles. If, for example, the concentrations used in the experiments were sufficiently high that particle coagulation would have been very rapid, it can be assumed that the animals were not actually exposed to ultrafine particles unless data are presented showing otherwise.

The chapter provides an extensive introduction to molecular dosimetry, but there is no effort to relate this information to possible mechanisms of action leading to the observed adverse health effects or effects at the tissue and whole organism level. If this information has any relevance to the standard setting process, there needs to be a clear description of how such information informs the exposure/effects relationships or the extrapolation of the high dose effects to likely effects at ambient concentrations.

Chapter 9 (Integrative Synthesis of Key Points: Particulate Matter Atmospheric Science, Air Quality, Human Exposure, Dosimetry, and Health Risks) requires major revisions. As EPA Staff noted during the meeting, there was insufficient time to really provide a truly integrated synthesis of the information in this chapter. The extensive discussion at the meeting along with our individual comments should provide assistance in revising this chapter from a summary to a synthesis.

We commend the EPA staff for the effort and attention to detail in preparing the current draft Criteria Document. We think it has brought together a wealth of new information and serves as a sound basis for a revised version that we look forward to reviewing in the near future. We look forward to your response to our advice.

Sincerely;

/ Signed /

Dr. Philip K. Hopke, Chair
Clean Air Scientific Advisory Committee

REFERENCES CITED

CASAC. 2000. Review of the Draft Air Quality Criteria for Particulate Matter. US EPA Science Advisory Board, Clean Air Scientific Advisory Committee (CASAC), Washington, DC February 15, 2000.

Court of Appeals. 1999. American Trucking Associations et al. vs. US EPA, 97-1440, US Court of Appeals for the District if Columbia Circuit.

EPA. 1999. Air Quality Criteria for Particulate Matter. US EPA Office of Research and Development (ORD), EPA 600/P–99/002a, Washington, DC, October 1999.

EPA. 2001. Air Quality Criteria for Particulate Matter (Second External Review Draft). US EPA Office of Research and Development (ORD), EPA 600/P–99/002bB, Washington, DC, March 2001.

Michaels, R.A. 1996. *Airborne Particle Excursions Contributing to Daily Average Particle Levels may be Managed via a 1 hr Standard, with Possible Public Health Benefits.* Aerosol Sci. Technol. 25:437.

Morgan, G.; Corbett, S.; Wlodarczyk, J.; Lewis, P. 1998. *Air pollution and daily mortality in Sydney, Australia, 1989 through 1993.* Am. J. Public Health 88:759-764.

NAS. 1999. Research Priorities for Airborne Particulate Matter - I - Immediate Priorities and a Long Range Research Portfolio. National Research Council. National Academy press, Washington, DC 195p.

Samet, J. M.; Dominici, F.; Zeger, S. L.; Schwartz, J.; Dockery, D. W. 2000a. *National morbidity, mortality, and air pollution study. Part I: methods and methodologic issues*. Cambridge, MA: Health Effects Institute; Research Report no. 94.

Samet, J. M.; Zeger, S. L.; Dominici, F.; Curriero, F.; Coursac, I.; Dockery, D. W.; Schwartz, J.; Zanobetti, A. 2000b. *The national morbidity, mortality, and air pollution study. Part II: morbidity, mortality, and air pollution in the United States*. Cambridge, MA: Health Effects Institute; Research Report no. 94.

Simpson, R. W.; Williams, G.; Petroeschevsky, A.; Morgan, G.; Rutherford, S. 1997. *Associations between outdoor air pollution and daily mortality in Brisbane, Australia*. Arch. Environ. Health 52:442-454

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EPA Science Advisory Board
Clean Air Scientific Advisory Committee
CASAC Particulate Matter Review Panel*

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a. SAB Members: Experts appointed by the Administrator to serve on one of the SAB Standing Committees.

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APPENDIX A - INDIVIDUAL PANELIST WRITTEN COMMENTS

Note: These are the final written comments provided by individual Panelists following the July 23-24, 2001 meeting. They are included here to present the full range of opinion and to document all edits suggested by Panelists. These are individual comments and do not necessarily represent the views of the Clean Air Scientific Advisory Board (CASAC) nor the EPA Science Advisory Board (SAB).

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* Did not attend the July 23-24, 2001 meeting.

Philip Hopke, PhD

Guiding Principles
There are two major questions facing EPA with respect to PM standards. First, they cannot have both a PM_{10} and a $PM_{2.5}$ standard. There can be one or the other. Thus, what science is available to help make this choice. One suspects that the answer is that there is more scientific support for a $PM_{2.5}$ standard.

This leads to the second issue: Should there be a standard for larger particle sizes? If so, what should be the indicator, concentration, averaging times, and statistical form of the standard? Thus, there needs to be a clear summary of the science that is or is not available to answer these questions

The current document is much too diffuse in its focus and fails to provide enough real evaluation to provide clear statements of what is and is not know about the health and welfare effects of various components of the ambient aerosol.

Chapter 2
Page 2-2, Lines 9-15: Complements on the good definitions.

Page 2-13, Line13, Prior to **1987** (not 1997)

Page 2-17, lines 2 to 15, There needs to be discussions of the nucleation events that are being observed by several groups (O'Dowd; Kulmala) of nucleation events. Most have been reported for remote areas like Macehead and Hyytila, but Kulmala has indicated to me that they have seen such events in Helsinki and it may be that McMurry has also seen them in Atlanta. Thus, homogeneous nucleation can be an important process for new particle formation although the details need to be investigated.

Page 2-18, lines 1 to 7: Kulmala suggests that ternary nucleation with NH_3 along with sulfuric acid and water is necessary to observe nucleation events. This is mentioned in their Nature article from last year. I can provide other references if needed.

Page 2-72, lines 7-12: The CASAC Subcommittee on Particle Monitoring has raised questions about the process of demonstrating equivalency for continuous monitors and the need to greater flexibility in bringing new technology into the compliance monitoring program. There needs to be some recognition of these problems here.

Page 2-72, lines 14-23: The 1996 CASAC PM Monitoring Subcommittee recommended a performance standard rather than a design standard. The fact that EPA made the PM_{10} criteria too loose does not mean that a performance standard would not work. It would not be as stifling on technology development.

The discussion fails to really highlight the fact that the FRM provides high precision measurements of totally unknown accuracy with respect to airborne particle mass concentration. It is time to face the need to really define what you want to measure and it should not simply be duplicating measurements made with dichotomous samplers that have now been discredited as being adequate for measurement of $PM_{2.5}$. The whole FRM program is full of contradictions and false assertions.

The discussion fails to discuss the need to greater time resolution in mass measurements. Right now we have no idea what the proper time interval is for setting a standard. We use 24 hours because that is what has been measured, but this interval has no basis in health effects.

Page 2-77, line 19-22: Should mention new developments in Synchotron XRF. It appears to have much higher sensitivity that will permit much higher time resolution.

Page 2-81, lines 5 and 6: The uncertainties in the reported slope and intercepts should be reported. There should always be uncertainty estimates with any reported data or data analyses.

Page 2-82, line 6: There are a number of references to papers in the PM2000 issue of *Aerosol Sci. Technol.* This issue was published in January 2001 and thus, all of these references like Chow *et al.* need to be updated.

Page 2-88, line 20: Same date problem. Also need to point out why we want better time resolved data. We have been adjusting the time interval of the O_3 standard because we have the data to aggregated the data at various time intervals. We do not have that advantage with PM unless "continuous" monitors are more widely used.

Page 2-94, lines 1-10: Fergenson *et al.* (In press, 2001) have shown that quantitative estimates can be made of the aerosol composition from the single particle MS data.

Page 2-96, lines 1-12: Need to add the Continuous Sulfate Monitors that are now available.

There is no discussion of measurement methods for Coarse particles and how you would get samples that could be used to characterize the particle compositions, do source apportionment, etc.

Chapter 3.
There needs to be a clearer focus on what is know about the concentrations, sources, distributions, compositions of coarse particles. There is too much emphasis on PM_{10} and not enough on coarse. Chapters 4 and 6 single out the effects of coarse. This chapter needs to coordinate with the background atmospheric behavior so that the context for the subsequent chapters has been created. There is only a short section on Page 3-11. If this is all the information that is available, then there has to be a clearer statement that information on $PM_{10-2.5}$ is limited and that this is all there is that is known regarding its distribution nationwide.

Page 3-19, Because of the very large variability in the relative amounts of fine and coarse particles, it is misleading to provide only a mean $PM_{2.5}/PM_{10}$ ratio. The only sensible way to provide such information is with distributions.

Page 3-26, lines 4 -10: Need to have the discussion of active homogeneous nucleation in Chapter 2 and need a pointer back to that discussion here.

Page 3-36, lines 10-21: A major part of secondary particles in the east and maybe elsewhere is secondary organic aerosol. Thus, there needs to be a discussion of the sources of the precursor gases that include both anthropogenic and biogenic sources.

Page 3-37, lines 23-31: Should add a discussion of UNMIX. EPA has invested in getting this model ready for use and should be included in this discussion.

Page 3-42, lines 11-28: This discussion is out of date. More recent data suggests a much more important role for SOA in the eastern US ambient aerosol.

Page 3-51, lines 8-11: Agriculture is a major source of ammonia. Take for example the Chino feedlot. With dairy farming widespread in the NE and North Central US, it could be important in the eastern US as well.

Page 3-54, lines 10-15: Point out that CEMs are available to look at SO_2. Other pollutants could be done if it were important (like needing verification for trading rights).

Page 3-55, lines 18-21: Later in the chapter, it is pointed out that the EI gives average emissions rather that the specific emission rates needed for modeling. It would be better to start that discussion here.

Page 3-56: Biogenic sources are important for precursors for SOA. What is known about those emission inventories. How good is BIES?

Chapter 4
This chapter should be complemented for making clear distinctions between the effects of fine and coarse particles.

Page 4-8, lines 19-28: The outflow of Asian dust to the mid-Pacific is now thought to be a critical source of micronutrients to the phytoplankton there. There should be a note of the work of Bob Duce and coworkers in this area.

Chapter 5
This chapter is very weak on describing what is known regarding the exposure to $PM_{10-2.5}$. Since Chapter 6 highlights the epidemiology of $PM_{10-2.5}$ separate from $PM_{2.5}$ and PM_{10}, it is important that there be parallel coverage of the exposure in this chapter to set the scene for that discussion.

Page 5-54- 5-55, What can be said more definitively about the penetration efficiency of $PM_{10-2.5}$? How does this affect our ability to relate $PM_{10-2.5}$ to total exposure and thus to adverse health effects? There needs to be a focused section on this issue comparing and contrasting the difference between $PM_{10-2.5}$ and $PM_{2.5}$ in this respect.

Pages 5-66, lines 23 - 26: UNMIX is rather different from PMF. It uses an eigenvector analysis which has been shown to provide non-optimal data point weighting because it fundamentally assumes homoscedastic data that is generally a poor assumption.

Page 5-92, lines 14 to 20: Is this discussion only about $PM_{2.5}$ or about both $PM_{2.5}$ and $PM_{10-2.5}$

Page 5-92, lines 25-31: Because of the poorer penetration of coarse particles and the much larger spatial inhomogeneities, there will be much larger errors in the exposure estimates for coarse. There needs to be a discussion of this problem here.

Chapter 6
Given the variability of $PM_{2.5}/PM_{10}$, there needs to be a discussion of whether or not the study of PM_{10} will really provide any insights into the quantitative risk assessment of $PM_{10-2.5}$.

Chapter 7
No comments

Chapter 8
There is no real discussion of organic aerosol mechanisms. The work that has been done is very important and useful, but there are other types of particles particularly primary and secondary organics. Since we can only separate and identify the specific compounds in about 20% of the organic mass under the best of conditions, it makes it very difficult to fully characterize the toxicological properties of these particles. It is very difficult to generate secondary organic aerosol in the lab and thus, providing reproducible conditions for exposing animal models is difficult.

Page 8-1, lines 26-28: Combustion aerosol are rarely "dominant" particle types. In most of the country, the dominant fine particle types are secondary aerosols. They do often derive from combustion generated SO_2, NO_x, and some organic compounds, but there are also important biogenic precursor compounds. Thus, there needs to be some rewording of this sentence.

Page 8-87: There is no separate discussion of the toxicology of coarse particles even to say that nothing is know regarding the toxicology of such particles.

Chapter 9
Page 9-10, lines17 to 29: This data is very outdated. The needs to be examination of the extensive data showing the frequent presence of an Aitken mode in rural aerosols as well as the occasional nuclei mode as well.

Section 9.3 has no discussion of coarse mode sampling.

Section 9.3.2.3: why is there a discussion of spatial variability of $PM_{2.5}$ without parallel discussions of PM_{10} and $PM_{10-2.5}$?

Frederick Miller, PhD

Chapter 6 - General Comments:
The chapter in its current form represents an extensive review of the available literature from epidemiological studies on the effects of particulate matter. The organization of the chapter into the major subheadings is appropriate. As one reads the chapter, there is a tendency for the $PM_{2.5}$ effects to be discussed in great detail and for the conclusion to be drawn that $PM_{2.5}$ is of more concern than $PM_{10-2.5}$. However, as the chapter develops, studies are presented showing the potential for coarse particles to have an effect. The balance of this discussion should be examined in particular as it is brought forth to the synthesis chapter.

Throughout the document values of $PM_{2.5}$ and $PM_{10-2.5}$ are presented. However, the document fails to make clear when $PM_{2.5}$ is a derived measurement vs. a direct measurement. This is critically important for standard setting purposes as correlation analyses provide different weight of evidence on average values compared to direct measurement. To help the reader in evaluating the strengths of the different studies, under Study Description it would be of value to simply indicate if measurements on exposure levels are direct or derived measurements.

Specific Comments:

p. 6-20	The Schwartz (2000c) study in the table reports a $PM_{2.5}$ mean of 15.6 mg/m^3. The study was conducted using data from 1979 1986. Were $PM_{2.5}$ measurements available in the late 1970s? How was the mean for $PM_{2.5}$ arrived at?
p. 6-23	The entry for the Smith study under Results and Comments brings up the topic of threshold. No discussion of this study follows until page 6-247. It is not clear why the emphasis in the discussion of Table 6-1 should be restricted to multi-city studies, particularly when individual studies bring up topics that are important for standard setting such as the concept of threshold, the statistical averaging time, or additional potential sensitive subpopulations.
p. 6-53	The figure presented here shows that 10 of 13 $PM_{2.5}$ studies and 4 of 13 coarse mode studies show statistical significance. While this gives greater emphasis to the importance of both the fine and the coarse mode for standard setting, the discussion in the text does not bring this point out as strongly as it should be. For example, in the section on crustal particle effects on page 6-56, the studies are discussed with a tendency for not showing an effect and little discussion is involved for the four studies that did demonstrate effects of coarse mode particles.
p. 6-77, l. 8 26	The slant towards interpretation of $PM_{2.5}$ and relative dismissal of the importance of the coarse mode is continued in this section here on fine and

	coarse particle effects. The paragraph clearly comes across as there may be some PM coarse mode effects but they probably are specific in location and they may even be due to biogenetically-derived particles. In addition, the statements throughout the chapter reflect strong statements of $PM_{2.5}$ causing effects and then the statements around the coarse mode, i.e., PM_{10-25} use phraseology such as may also be important. This comes across to the reader as a bias of the authors relative to fine vs. coarse mode effects. This tone is continued on page 6-78, l. 2 4 where the statement is made that crustal particles do not appear overall to support associations with mortality in the source oriented evaluations. While clear recognition must be given that there are more studies demonstrating the importance of $PM_{2.5}$, the dismissal of coarse particles in the presence of positive studies is disconcerting, particularly given that much of the western part of the United States has PM_{10} dominated by the coarse mode fraction.
p. 6-84, Table 6-6	In the cardiopulmonary mortality column for the six cities original vs. the HEI reanalysis, a consistency of the point estimate is what one would expect. However, the much larger difference in the confidence limit bounds is surprising. It would be worth checking the entry in this table to ensure that a typographical error has not occurred.
p. 6-105, l. 11 26	The actuarial and statistical calculations presented based upon Brunekreef are hard to believe. The implication that the life span of persons exposed to and dying from air pollution is a reduction of more than 10 years, if true, would surely have been detected without the kind of sophisticated statistical analyses that are currently being required. In addition, what exactly is meant by implying that up through age 25 a loss of 1.31 years occurs for the entire population? Is this life span reduction? If so, actuarial numbers likely contradict this conclusion.
p. 6-107, l. 17	The conclusion from the Krewski et al. study that mortality may be associated with more than one component of the complex of ambient pollutants in urban areas bears emphasis in the synthesis chapter and is appropriately highlighted in various sections of the epidemiological discussions.
p. 6-107, l. 30	The mortality log hazard ratio increasing to 15 mg/m^3 and then being flat before continuing to increase again, while being a statistical model that appears to fit the data, has little biological motivation to support it (i.e., such a model makes little biological sense).
p. 6-108, l.8 13	The Krewski et al. study looking at the relative risk and incorporating time-dependent estimates is particularly important for the standard setting process. EPA must factor the temporal decline in PM that has been occurring in its assessment of the need for revisions of or new standards for particulate matter. This is particularly important with the various implementation strategies that have yet to take effect that are clearly leading to a reduction in overall pollution levels in this country.
p. 6-205, l. 10 19	A number of studies on long term effects from PM are cited as having been conducted in California but with inconsistent results. Yet the authors choose to describe the McConnell study as the most notable because it showed an increase that is similar to results reported by Dockery. Why is this study notable? It appears the authors have considered it such because it found effects when others didn t. This does not appear to be a balanced representation and discussion of the newly available studies.
p. 6-230, l.17 20	The nonlinear model for fine PM effects in the study by Smith et al. is of potential interest since a threshold between 20 25 mg/m^3 for $PM_{2.5}$ was seen in this study. Has the type of model presented by Smith et al. been applied in other data sets?
p. 6-247, l. 25	The summation of the Smith study relative to threshold selection and importance of fine vs. coarse is phrased as these results, if they in fact reflect reality, make it difficult to evaluate the relative role of different PM components One might interpret the authors use of the phrase if they in fact reflect reality as a bias for wanting to attribute one of the two modes as being more important. Alternatively, the sentence is an excellent summary of why the PM issue is so entangled and difficult to separate on a causative basis for one

mode vs. the other. In fact, such kinds of difficulties are precisely why the Agency must look carefully at standards for PM that encompass the full spectrum of potential effects in different locations.

Chapter 7: Dosimetry of Particulate Matter - General Comments:

Chapter 7 on the dosimetry of particulate matter primarily focuses on an update of new studies since the 1996 Criteria Document (CD). While the chapter provides a reasonable review of the available literature, the review is lacking in details in a number of areas. Given the importance of and reference to dosimetry considerations elsewhere in the document, the chapter should be strengthened with more specific presentations of some of the latest results.

The chapter fails to take advantage of a graphical representation of the more recent data. Such graphical representations covering susceptible subgroups in comparison to normal subjects would be of great value. The authors failed to report whether increases compared from one group to another are actually statistically significant or just represent general trends. Without showing the data and the standard deviations or error bars, the reader is left with a general uncertainty about the significance of any differences that are reported.

Section 7.5 on the comparisons of deposition and clearance patterns of particles administered by inhalation intratracheal instillation adds little to the chapter. This section, while accurate, is of little value for the risk assessment of particulate matter. There is no mention of the role that intratracheal administration can play in hazard identification and in mechanism of action studies. If this section is retained, clearer identification of the value of the animal toxicological studies using this method should be discussed. This is particularly important since many of the studies presented in Chapter 8 on animal toxicological results arise from intratracheal administration experiments. Section 7.5 should be reduced in size if it is retained.

Detailed tables or graphs contrasting deposition in children compared to adults should be presented in the chapter. Since arguments are made elsewhere in the CD about children being a potential susceptible population, dosimetric differences between children and adults need to be presented in greater detail than they currently are. The logic of having the only figure in the dosimetry chapter be one of total deposition is not apparent. While such data are of general interest, the types of effects and standard setting concerns focus on the major regions of the respiratory tract. Regional deposition should be presented and should incorporate recent research on different subpopulations and disease groups.

Specific Comments:

p. 7-2, l. 16	The reference to information related to the phenomenon of particle overload is stretching the case for inclusion of this material. Clearly, there are no ambient exposures of particulate matter that approximate anything close to the exposure levels needed to induce overload of alveolar macrophage-mediated clearance that is the basis for this phenomenon in animals.
p. 7-5, l. 7 11	The authors should clarify that the importance being described for various deposition mechanisms in respiratory tract regions applies to humans. The importance of some of these mechanisms differs on a relative sense for some and on an absolute sense for others when referring to particle deposition in animals.
p. 7-6, l. 21 27	The cast studies with charged particles are not very relevant to real world ambient aerosols. If this material is retained, a better explanation of where these results might be applicable for potential real world exposures should be provided.
p. 7-7, l. 6 16	It is important in this paragraph to contrast inhalability in humans compared to inhalability of particles in animals. Otherwise the reader has no insight as to why this is an important concept to introduce and further has no reference for determining some of the relevance of concentrations used in animals when judging the potential for effects in humans.
p. 7-8, l. 1 7	Of value would have been to compare the recent results of Kim to those previously published by the GSF group for various combinations of tidal volumes and respiratory frequencies.
p. 7-10, l. 14 19	Since the study by Lenin used a fairly narrow size range (0.3 2.5 mm), the

	statements concerning particle size and flow rate and various breathing modes, while accurate, should be stated in such a way that the reader understands that these conclusions do not hold for a wider range of particle sizes.
p. 7-13, l. 24	The study by Kim and Fisher using sequential double bifurcation tube models, while yielding interesting results, should be put into perspective given that downstream flow affects deposition in the whole lung and is not necessarily approximated by sequential series of double bifurcation models.
p. 7-14. l. 26	The study by Venkataram and Kao 1999 used totally unrealistic breathing conditions in that they assumed breathing for 24 hours at conditions that are not physiologically sustainable. Only general trends can be inferred from their calculations as the quantitative values are not useful.
p. 7-15, l. 25	The paragraph beginning with this line should be reworked. The statements made in this paragraph are inconsistent with earlier statements of a decrease in deposition for particles with an initial diameter less than 0.5 mm and an increase in deposition with an initial diameter greater than 0.5 mm.
p. 7-17, l. 21	A gender difference of about 15% at rest for particle deposition is stated for the studies of Kim et al. Was the 15% change statistically significant? Without this information the reader can t really interpret the significance of the findings.
p. 7-19, l. 18 30	The way the Bennett et al. study is presented the reader cannot really judge the importance of the reported data. on ET deposition. ET deposition as a percentage of total respiratory tract deposition is the basis for making statements about differences in percentages. While these differences are statistically different, they are restricted to 4.5 mm particles since this was the only particle size Bennett et al. studied. However, the statement in the CD about the trend for ET deposition tending to increase as age decreased is not a statistically significant observation. The contention that the deposition seen in the cystic fibrosis children studied by Bennett et al. likely reflects what one would expect in normal children is suspect. The argument presented by Bennett et al is not convincing in that just because lung deposition is expected to be increased in cystic fibrosis children does not infer that ET deposition would tend to be decreased in these kids. Since ET deposition is upstream relative to lung deposition, one can not infer the negative (i.e., increased lung deposition does not confer that ET deposition should be decreased in cystic fibrotic children compared to normal children).
p. 7-20, l. 12 15	Again, are the differences reported statistically significant?
p. 7-24, l. 3 10	Recent results published by Asgharian et al. (Aerosol Sci. 32, 817 832, 2001) also support the influence of lung size on the retention of particles in the tracheobronchial region for periods longer than 24 hours after deposition.
p. 7-27, l.10 22	The way the paragraph comes across in describing the results in Musante and Martonen to infer that the rat may not be a good model for the resting human masks the fact that one has to account for differences in doing interspecies extrapolations. To make the argument that a greater activity level yields a more similar distribution of dose on a regional basis does not necessarily imply that this mode would be better since, for example, the distribution of types of cells within the respiratory tract differ by airway generation between the rat and the human. This paragraph could be expanded upon to point out some of the differences that must be taken into account when extrapolating between species.
p. 7-29, l. 20	Rather than starting the sentence with the phrase for the most part , the author should indicate that for hygroscopic particles and liquid droplets, clearance mechanisms are different compared to poorly soluble particles.
p. 7-34, l. 25	Asgharian et al. (Aerosol Sci. 32, 817 832, 2001) recently showed that it is not necessary to invoke a slow- and a fast-phase for tracheobronchial clearance to have particles retained in the TB region longer than 24 hours. Intersubject variability in retained mass arising from the periphery of the TB based upon lungs with variable number of airways can explain the experimental observations while still fitting a single compartment clearance model.
p. 7-40, l. 4 7	References should be supplied to support the statement made in this paragraph.
p. 7-40, l. 14	Physical activity is not really a biological factor in comparison to the other subsections covering age, gender, and the like. Why not simply entitle Section 7.3.4 Factors Modulating Clearance?

p. 7-49, l. 20	In an effort to make the chapter brief, the authors have indicated that additional work on modeling deposition in animals has been published but that it merely expands on work and approaches already noted in the 1996 PM Criteria Document. The text would leave most readers with the idea that the additional work is not of value. Since the work of Hoffman et al. (2000) is described on the next page, surely the inference is not that this is the only work that has made additional contributions. Some of the features and some of the additional references should be included here to provide a perspective on what the thrust of the additional work has been. To merely say that it has expanded upon previous work is not sufficient. For example, recent experimental and modeling work on particle deposition with pulsating flow in a rat nasal mold by Asgharian et al. (Inhal. Toxicol. 13: 577-588, 2001) demonstrates that deposition efficiencies for pulsating flows are markedly higher than for steady flows.
p. 7-50, l. 7 12	The statement that models have not been adapted to examine low level exposures to particles of low toxicity and poor solubility is incorrect. Koch and Stöber (Inhal. Toxicol. 13: 129-148, 2001) published a pulmonary retention model that accounts for dissolution and macrophage-mediated removal of deposited polydisperse particles. Their model and the results arising therefrom should be discussed.
p. 7-50, l. 13	The Asgharian et al. reference has the incorrect year. 2000 is cited in the text, but the correct year is 1995.
p. 7-51, Section 7.6.2	There does not appear to be a compelling reason that a separate section should be devoted to models that estimate retained dose. Estimation of retained dose is a natural extension of models that handle both deposition and clearance processes. The material discussed in this section should be integrated into the clearance discussion because the various topics that are presented form the basis of clearance models of varying degrees of sophistication depending upon how much is known about the biological process.
p. 7-52, l. 25	Strike recently, from the sentence describing the work of Nikula et al. (1997). The year 1997 is no longer recent compared to 2001.
p. 7-52, l. 22 31	This paragraph lacks a punch line. While interspecies differences in interstitial translocation and retention of particles is established, the statement is made that these interspecies differences may not occur at low levels of exposure. What is the justification for this statement? Are there any references to support this conclusion?

Chapter 8: Toxicology of Particulate Matter - General Comments:

Since toxicological studies are presented for both animals and humans, the title of this chapter should reflect such. In the past, toxicology has been usually restricted for description of animal results. This chapter provides a reasonable summation of the findings of studies that have been conducted since the 1996 Criteria Document. Unfortunately, as reflected in the summary, the biological plausibility of various constituents and mechanisms of action for effects are still not clearly established.

Section 8.5 of the chapter is labeled as Mechanisms of PM Toxicity from In Vitro Exposures. In actuality much of the material presented is simply effects from in vitro studies and really not insightful on mechanisms of actions of PM. The organization of the chapter in this way begs the question as to whether any mechanistic insights have been or can be gained from in vivo studies. Since I do not think that is the intent, cross referencing to in vivo and inhalation studies that correlate types of responses or effects seen with those in in vitro studies should be made whenever possible.

Specific Comments:

p. 8-9, l. 19 22	The statement is made that it is not clear that the total dose of iron oxide delivered acutely to the lungs of human subjects would be relevant to deposition of iron given its concentration in ambient environment. A much stronger statement can be made. Just consider a minute ventilation of 15 liters per minute. Doing the calculations for 1 mg/m^3 in the air, the amount instilled bears no semblance to reality of what could be deposited in any reasonable acute exposure to these levels (e.g., assuming no clearance of particles and 100

	% deposition, more than 7 months would be needed to deposit 5 mg of the iron oxide particles in the lung since only about 20 mg would be deposited in a day).
p. 8-16	The concentration stated in the table for the Madden et al. study should be 1000 mg in 0.5 ml.
p. 8-17	For the Watkinson et al. study, what were the nose-only inhalation concentrations?
p. 8-18, Table 8-5	Given the low exposure of 10 mg/m^3 for 4 hours in the Ohtsuka et al. study, this paper warrants expanded discussion in the text.
p. 8-24	The symbol for the geometric standard deviation is not as it appears in the table but rather should be the Greek symbol s. The same statement can be made for Table 8-7.
p. 8-28, Table 8-7	This reviewer finds it of great interest that intertracheal instillation of ROFA in the Watkinson et al. study showed effects but inhalation of 15 mg/m^3 six hours per day for three days of the same compound showed no effects.
p. 8-29, l. 11 20	In the Killingsworth et al. Studies using monocrotaline-MCT, mortality and changes in MIP-2 were noted. What human condition does this model mimic?
p. 8-32, l. 6 19	This paragraph comes across as if the Godleski et al. HEI Report is considered peer reviewed and the study by Muggenberg et al. appearing in an *Inhalation Toxicology* Supplement from the PM 2000 Meeting is not peer reviewed. The fact that these studies differed in their findings is what should be emphasized because Godleski used concentrated ambient particles and Muggenberg used high concentrations of ROFA. If EPA has criteria for what the agency considers peer reviewed versus not peer reviewed, these criteria should be so stated and applied uniformly throughout the Criteria Document.
p. 8-31, l. 18 19	The statement is made that the different findings between the dog studies illustrate the difficulties in extrapolating animal toxicological data to human health effects. The sentence falls short in that it fails to note that lack of understanding of mechanism of action is the primary problem with extrapolating animal results that are disparate in nature to humans.
p. 8-33, l. 6 9	The results from the Gordon et al. study are interpreted in this paragraph to suggest that day-to-day changes in particle composition may play an important role in the systemic effects of inhaled particles. This is an overinterpretation of
p. 8 34, l. 4 14	In addition to the potential mechanisms discussed in this paragraph, the role of endothelins should be mentioned. Vincent et al. (Inhalation Toxicology of Ambient Particulate Matter: Acute Cardiovascular Effects of Resuspended EHC-93 Urban Particles in Wistar Rats. Final Report to the Health Effects Institute for the Collaborative Study 98-32, In Press, 2001) have shown that particles can affect endothelin 1 and 3 more than 30 hours post exposure.
p. 8-37, l.10	Replace the word although with the word after.
p. 8-41, l. 18	Broad statements such as what Nell et al. made in their article on suggesting that the rise in the U.S. prevalence rate for allergic rhinitis may be related to increased diesel emissions in addition to other combustion sources is highly speculative. Anyone can suggest a material is the culpritive agent for an effect but the emphasis in a criteria document ought to be on the proof for such relationships based upon experimental data.
p. 8-46, l. 13	The astronomically high carbon black exposure level used by Jakab produced no effect on susceptibility to bacterial infection in contrast to high exposure studies with titanium dioxide. Comparing such results implies that a particle is not a particle and that composition or the nature of the particle is important for the effects on the host. The Criteria Document does not put as much emphasis on pointing out concepts such as this as what might be appropriate.
p. 8-61, l. 3	Round 11.9-fold to 12-fold. Such rounding is undoubtedly more in accord with the accuracy of the data.
p. 8-62, l. 3	The concept discussed here that a combination of several components rather than a single metal in PM is likely responsible for cellular effects is worth bringing forward as one of the major conclusions that can be gained from examining the toxicological data on PM.
p. 8-67, l. 4	The Lee et al. studies described here involved sulfuric acid aerosol concentrations so high as to make the results of little value to the discussion of

ambient PM effects. The paragraph describing this study should be deleted.

p. 8-70, l. 3 — Insert the word to after the word shown.

p. 8-71, l. 5 24 — Perhaps the authors of this chapter would comment on the paradoxical outcome of results found by Churg contrasting fine and ultrafine particles. Is the rat tracheal explant model a reasonable one for making the kinds of comparisons that were done by Churg et al.?

Arthur C. Upton, MD

Transmitted herewith, as requested, are my comments on chapters 6 and 9 of the draft Criteria Document on PM. In general, I consider these chapters to be excellent, and I have no substantive changes to suggest on either of them. Both chapters do, however, need careful editing to deal with such problems as the following:

Pages 6-6, line 23 and 6-39, line 1: "most all" is ambiguous.

Page 6-267, lines 19-20: grammatically incorrect (words missing?).

Page 9-7, line 10: "this chapter and" should be deleted.

Page 9-8, last line: the reference to "Wilson and Suh" is missing from the bibliography, as are many of the other references cited elsewhere in the chapter.

Page 9-16, line 3: the second "is" should be changed to "are".

The effect of educational level on the relative risk of mortality (mentioned on page 9-65) deserves discussion at an appropriate place in the chapter.

The data suggesting an increased relative risk for lung cancer (mentioned on page 9-65) deserve to be included in the appendix and discussed at an appropriate place in the chapter.

In addition to editorial corrections such as those noted above, the document needs a glossary to define the many technical terms and acronyms that are used in these and other chapters.

Sverre Vedal, MD

Chapter 6. Epidemiology.
This chapter has been extensively revised and updated since the last version, and is much improved. The uneven treatment of the more recent studies in the previous version is now less evident, although persists to some extent (see below), and the very important studies supported by HEI (NMMAPS I & II, Reanalysis Project) have been thoroughly reviewed and incorporated into the synthesis. The **most important issues** are dealt with in the sections that immediately follow, with less important issues following.

1. Coarse fraction findings

As documented in the CD, much more observational data are available to address whether the fine PM fraction is more toxic than the coarse fraction. While some new studies found larger effects of the fine fraction, many new studies found at least comparable, and sometimes larger, effects for the coarse fraction: these include studies from Detroit (Lippmann 2000), from Phoenix (Clyde 2000, Mar 2000 & Smith 2000), the Coachella Valley in California (Ostro 1999 & 2000), and Seattle (Sheppard 1999), as well as the Latin American studies from Mexico City (Castillejos) and Santiago (Cifuentes). The general impression one gets from the CD is that new findings are generally supportive of the hypothesis that fine particle effects are dominant. Instead, I find the recent study findings, as a group, support an effect of coarse mode particles, and sometimes crustal particles regardless of size. At the time of the 1996 CD, there

was a dire need for studies assessing coarse particle effects directly. Now that findings from several are available, at the very least they show little consistency in supporting a dominant role for fine PM.

The CD attempts to undermine the validity of the observations in the studies in which coarse PM effects were detected, although the synthesis (p.6-229 (line 22)-230 & 235) provides a more balanced assessment. For example, the statement that "several [studies] do show statistical[ly] distinctly larger and significant mortality associations with $PM_{2.5}$ than for non-significant $PM_{10-2.5}$ effects" (p.6-54, line5-6) ignores the fact that several do not. And, while it may be true that no study has the power to adequately compare effect estimates sizes between the fine and coarse range, this has previously not prevented comparisons of effect sizes of many particle metrics that are highly correlated. In response to the Lippmann findings in Detroit it is argued that the coarse fraction findings are present because the coarse fraction is correlated with the fine fraction [6-55, line 10-11; 6-127, line 13-16]. In response to the findings in Phoenix it is argued that the apparent coarse effects may be due to biogenic particles in that fraction (6-55, line 27 & 6-77, line 22-26). This argument is speculative and should be framed as such. I also find it unlikely. None of the above arguments supporting a more toxic role for fine PM is compelling. Given the new data on coarse PM which were not available at the time of the last CD, it is difficult to argue strongly that fine PM effects are dominant, regardless of setting.

It is also my opinion that the conclusions regarding crustal effects (p.6-78, line 2-4 and 6-267, line 10-11) are too strong. Although the studies making use of factor analyses to attempt to attribute effects to various sources generally do not find much to support adverse effects of crustal sources (Laden 2000, for example), and some studies incorporating wind patterns in attempting to identify periods of large crustal contribution to PM (Spokane and Salt Lake City studies) argue against a crustal PM effect, it is difficult to ignore the findings from studies where PM is almost entirely crustal in nature (Anchorage, Phoenix (for coarse mode PM), Coachella Valley, etc.).

If the authors of the CD disagree with these assessments of coarse fraction effects and effects of crustal particles, at the least a better attempt at making the case should be made, preferably in the summarizing sections.

A small point: it is not appropriate to compare $PM_{2.5}$ and PM_{10} on a mcg per mcg basis (6-231, line 19-22).

2. Balance in review of relevant studies

There is still an unfortunate, and unnecessary, tendency in the body of this chapter to use a different (more stringent) yardstick in evaluating studies that report findings at odds with the favored hypotheses (PM effects are more consistent than gaseous effects; fine PM effects are stronger than coarse fraction effects). Some examples follow:

6-45 Most of the cities included in NMMAPS II only had every 6-day PM measurements, yet this is never brought up as a criticism, whereas this is identified as a weakness in the Moolgavkar study (2000) that stressed the importance of gaseous pollutant effects over PM effects.

6-101 Criticisms of the EPRI study are based on the argument that factors that are in the "causal chain" cannot confound an association, and that the population sample is unrepresentative. However, equally severe criticisms regarding lack of representativeness could have been leveled at the ACS study, but were not. The discussion regarding high blood pressure as a potential step in the development of PM-induced mortality is very much speculative and has no place in the description of this study. Why is it noted that the study has "no matched control or placebo" (6-100, line 14) when these are not relevant given the study design, and are not considerations for the other cohort studies?

6-127 The paradoxical findings from the first 5 years of the Atlanta hospitalization study are downplayed since the AIRS database is used for PM, whereas the more expected findings for one year using Supersite data are emphasized. Recall that NMMAPS made use of the AIRS database.

6-129 In reviewing the Burnett hospitalization studies in which effects of gaseous pollutants are

dominant, one criticism is that "best lags" were reported, yet this use of best lags is justified later (6-238). Almost all studies explore "data driven" lag structures.

6-131 It is bizarre that the mortality data are brought up in this section dealing with hospitalizations to "shore up" the argument for PM & cardiovascular effects.

6-134 Why does this summary only include the US studies, which incidentally are all "positive" studies, when important international studies, many of which are "negative" studies, are not included?

To summarize, rather than attempting to shore up favored hypotheses, and through doing so, revealing a bias, it would be preferable to do less editorializing during presentation of studies, and stand back for a more objective look at the studies as a whole. This is what we expect from a CD.

3. Confounding

Confounding remains an issue of concern. In the time-series studies, concerns regarding meteorology, in the absence of more innovative approaches to specifying the form of meteorology in the time series regression models, can probably be put to rest given the many attempts to incorporate alternative specifications without significant impacts on the PM estimates of effect. The CD is probably correct in this regard.

Confounding by co-pollutants, a perennial concern, has also been addressed in the CD. Several points should be noted. First, it is correctly noted that effects based on attempts to control for confounding in two-pollutant or multi-pollutant models are often difficult to interpret because of the typically strong between-pollutant correlations that are present in the time-series studies. However, this does not imply that effects from single-pollutant models of PM are unconfounded estimates. The findings regarding PM effects, as well as estimates of PM effect in the CD, are largely reported only from single-pollutant models (as one example, p.6-142, line 17). Second, results from various alternatives to the use of multi-pollutant models in estimating PM effects unconfounded by co-pollutants are presented. These approaches are motivated by frustration at interpreting PM effects from multi-pollutant models. In NMMAPS II gaseous pollutant effects were controlled in a second stage (multiple city) analysis after the individual-city single-pollutant PM effects were estimated. This is probably justified in this setting given the relatively large number of cities included, although it seems difficult to imagine that adequate control for co-pollutants could be adequately accomplished without attending to the seasonal variation in co-pollutant concentrations, variation that itself differs from region to region across the country. A different approach to addressing potential confounding by gaseous pollutants is exemplified by the multi-city hospitalization studies, including NMMAPS II (Schwartz 2000, Zanobetti 2000). Firstly, the description of these methods is difficult to follow in the CD narrative (6.223-225). Descriptions of these alternative approaches to accounting for co-pollutant effects are difficult to follow. I still cannot figure out the rationale behind some of these approaches from reading this section, which may mean that others cannot either. Clearer rationale for the specific approaches taken is needed. Parenthetically, I wonder whether the correct correlation (r) between PM and the co-pollutants should be the correlation after adjusting for long-term trends and meteorology (that is, correlations between the effect estimates rather than raw correlations). Secondly, we have much less confidence in the success of this approach given the much smaller number of cities (and often smaller size of cities [e.g., Boulder, Youngstown) used for these analyses. The CD seems to uncritically accept this approach to controlling confounding by the gaseous pollutants (6-126, line 4, for example).

There has been discussion of the potential for the gaseous pollutants to confound the association between PM and health effects from the perspective of the definition of confounding. It is argued that some of the co-pollutants cannot be viewed as confounders since, based on biomedical knowledge, they should not affect the outcomes of interest. Neither SO_2 , sulfate nor CO can reasonably be argued to cause many of the effects with which they are often associated. It would be true that these pollutants could not confound if in fact the ambient co-pollutant concentrations were truly measuring exposure to these specific pollutants. Realistically, however, they do not. The co-pollutants are likely measuring various aspects of the pollution-meteorology mix and acting as surrogate measures of important exposures that we do not now

understand. Further, PM is qualitatively no different than the gaseous pollutants in this regard. Therefore, it still makes sense to consider the gaseous pollutants as potential confounders of PM. Similarly, attempts to stop considering some of the co-pollutants as confounders, arguing, as is done in the CD, that they are merely steps in the mechanistic causal chain (see below), are not valid.

4. Regional heterogeneity

The emphasis in this CD on NMMAPS II is justified. The heterogeneity in the estimates of PM effect across US cities is obvious (28 of 88 cities having non-positive estimates of effect). This is the first good impression available of the degreee of heterogeneity that is present. The heterogeneity might be due to random variation in estimates of effect (presumably supported by the CD in developing the argument that in general the absence of effect is observed for cities with fewer observations, i.e., less power), or it may represent true regional differences. It should be noted that the heterogeneity observed in the NMMAPS II study of 88 cities is present for single-pollutant models. PM effects from two-pollutant, or multipollutant models, would be expected to have shown even more heterogeneity among the cities. Further, interpreting the meaning of an estimate of overall effect (0.5% increase for a 10 mcg/m^3 increase at lag 1) assumes that the effects across city come from a single distribution of effects, which might not be the case if heterogeneity of effects is real and due to some as yet to be identified factor(s) that distinguishes cities in which effects are detected from those in which they are not. The cause(s) of this apparent heterogeneity (random variation or "real") clearly has implications for setting US-wide, health-based standards.

An attempt is made to explain part of the observed heterogeneity of effect by noting that negative or absent effects were more likely to be seen in cities with the lower concentrations of PM (6-263, line 30-). This is unjustified given that the NMMAPS investigators explicitly tested that hypothesis and found no support for it.

5. Chronic effects

Although the cohort studies are invariably referred to as studies evaluating the effects of "long-term", or "chronic", exposure, this is an assumption. The title of section 6.2.3 ("Mortality Effects of Long-Term Exposure to Ambient Particulate Matter") already makes this assumption. Merely because exposure in these studies is specified in terms of long-term averages, this does not imply that the observed associations are in fact due to these long-term averages. An alternative is that these effects are simply a cumulation of acute effects. It is argued that simple accumulation of acute effects cannot account for the size of effects estimated in the cohort studies. However, these estimates are somewhat sensitive to covariates and analytic approach (e.g., adjustment for population mobility, spatial correlation and control for SO_2 as demonstrated in the ACS Reanalysis Study). Therefore, confidence in the size of these reported effect estimates is not great. Reflecting even more confusion is the statement in the CD (p.6-80, line 31) that chronic effects must be present since effect estimates for chronic PM exposure are much higher than those for the time series studies; this point is irrelevant and in no way argues that a chronic effect above that observed in the time series studies must be present (this is an "apples and oranges" comparison). The comparison of the spatial features of effects from NMMAPS II and the Cohort Reanalysis Project (6-265, line 24-31) does not necessarily enhance the argument for consistency, given the above.

Effects of acute exposures can theoretically be approximated by calculating a cumulation of acute effects, something which has been attempted previously. I recommend revisiting the issue of cumulating time series effects (incorporating the impact of multiple days) to compare to the range of estimates of PM effect from the cohort studies (esp. the ranges of effects estimated in the ACS reanalyses based on different models). If this argument is convincing in showing that acute effects could not conceivably reproduce findings from the cohort studies, then the above points become moot. The lung cancer findings, if valid, would provide a strong argument for chronic effects, but this discussion is largely lacking from this version of the CD.

In my opinion, given the above, the conclusion regarding "long-term exposure to PM" (6-94) needs to be qualified.

6. Susceptible sub-populations

It is surprising that the most important study to date on identifying susceptibility of populations subgroups based on pre-existing medical disorders is discussed so little (Goldberg 2000), being presented last in a discussion of previous studies that, because of design, are limited in the information that they provide in this regard. This study confirms many of the findings of studies that attempt to address the issue by stratifying on cause of death. However, it is interesting that no increased risk was identified for the subgroup of subjects with chronic obstructive lung disease, a group considered to be at high risk based on cause-of-death stratifications. Parenthetically, I believe the description of the Goldberg study gets it wrong. PM pollutant measures were associated with mortality, not with acute respiratory disease, etc. (p.6-74, line 24-30) as stated. The latter were the susceptibility subgroups (that is, for assessing interaction effects, essentially).

There is legitimate concern that the stratification of by cause of death is fraught with problems misclassifying

7. Miscellaneous "large" issues

Gaseous pollutant effects: The summaries provide relatively balanced syntheses of recent gaseous findings (p.6-75, line 14-23 & p. 6-76, line 24-). This balance is sometimes lacking in the descriptions of specific studies in which a "particle-centric" perspective is maintained (see point 2 above). For example, the conclusion that fine PM effects on cardiovascular hospitalizations are most important (6-235, line 1) ignores the important findings by Burnett and Moolgavkar on the role of gases in affecting estimates of PM effects.

Threshold concentrations: The discussion of thresholds is unconvincing. The argument attributed to Schwartz that a threshold is mathematically impossible in the face of population differences in sensitivity (p.6-246, line 3-5) holds only if the most sensitive members of a population are sensitive to very low concentrations, which may not be the case. Further, the CD is not consistent in its support of a no-threshold concentration-response relationship. The argument that heterogeneity in studies of PM composition is due to variable concentrations of PM components (with studies showing no effects having concentrations too low to show effects, 6-78, line 1) is not consistent with the absence of thresholds. The same point can be made if heterogeneity of effects in NMMAPS is argued to be due to variability in PM concentrations across city (see point 4 above).

Measurement error: The description of the Zeger (2000) work on measurement error (6.249-252) is just about comprehensible. "Dumbing" this section down, if possible, would be allow it to have the impact that it deserves.

Smaller issues for chapter 6 (by page number):

Introduction

6-2 I don't believe Rothman would assign more inferential strength to case-control studies than cohort studies (line 14).

6-3 The prospective cohort studies in this setting do not make use of "individual exposure" (line 2). The subjects in a cohort study do not need to be recruited independent of exposure (line 4), and in fact were not (e.g., 6-Cities Study).

6-4 Line 19-25. The discussion of causal pathways, although correct, is not relevant in this context. Because SO_2 contributes to sulfate formation does not imply that SO_2 effects cannot be separated from sulfate effects, if correlations are not too strong. But, this is an issue of collinearity.

6-5 One gets the impression here that meteorology is acting solely as an effect modifier (line 1), when in fact the more important issue is its role as a potential confounder (see "Confounding" section above).

Mortality

6-6 Line 25-26. "Statistically independent" is unclear here. Like for effects due to infectious illnesses, respiratory and cardiovascular causes can be difficult to entangle, and can be caused by the same insult.

6-9 Line 26. It would seem that harvesting could be more readily addressed in the context of "identifiable PM episodes" than the typical time-series studies in which only day-to-day variability in concentration is studied. Is it being suggested that low level exposure may have a different lag profile?

6-40 Line 14. Should be "88" cities.

6-42 Line 5-6. On p.6-7, the reported reasonable range of effects from the 1996 CD is estimated to be 2.5-5.0% increase per 50 mcg/m^3. The 2.3% increase estimated in NMMAPS II is outside this range and therefore, strictly, not consistent. As noted, there were studies by 1996 showing statistically significant effects that were smaller than 2.5% (e.g., 1.8%), but that is not relevant. See also p.6-49 (line 19) and p.6-76 (line 3).

6-43 Line 6-7. We do not know from NMMAPS II whether a different tack to trying to account for gaseous pollutant effects (see above) on the PM estimates would have reached different conclusions.

6-44 Line 20-26. In the 10-Cities studies, the attempt to control for gaseous pollutant effects is severely hampered by lack of power (see point 3 above).

6-59 Line 26. This should be Table 6-3 rather than 6-1.

6-61 Table 6.3. The "single pollutant models" heading is confusing, since this includes 2-pollutant model findings.

6-62 Line 6. This should be Table 6-4 rather than 6-3.

6-78 The threshold discussion here is premature, since no studies presenting data on thresholds have been presented up to this point.

6-92 Why is a 20 mcg/m^3 increment used for both $PM_{2.5}$ and PM_{15}?

6-101 It is not clear why these studies of mortality in children and on development (IUGR) (6.2.3.4) are included in a section on purported long-term effects on mortality, nor why a time-series study (Loomis p.6-104) is included. I would argue with the descriptor "likely" (p.6-103, line 5).

Morbidity

6-125 Line 14. This is not strictly a subset of the 88 cities, I believe (e.g., Boulder?).

6-139 The Seaton study (line 26) also found a reduction in hemoglobin concentration in association with PM.

6-141 I would not consider the data on blood viscosity as "highly suggestive" (line), given the negative findings of several other studies including the more recent Seaton study (1999).

6-141 Line 9. It should be noted that effects at longer lags are often not investigated.

4-143 Line 25 to p.6-172. The point that the single "best" lag represents the most valid effect estimate, based on it being biased high but countered by not reflecting the full impact of multiple lags, is ingenious but nevertheless nonsense.

6-173 Line 8. Power for Edinburgh for hospitalization counts (but not for mortality) should be adequate.

6-175. Line 16. Why is the Sheppard study particularly "unique"?

6-176. Line 13-17. The effects of acid aerosol and PM should not be compared on a mcg per mcg basis.

6-176 Line 3. Asthma ER visit studies that complicate the argument about fine PM here include Lipsett 1997 from Coachella Valley on coarse PM and Chapela (year?) from Mexico City in which no PM effects were detected.

Interpretation

6-216 Line 25. Have some studies really looked at cardiac symptoms?

6-226 The argument that SO_2 cannot be a confounder of PM because it is part of the causal pathway is wrong in most settings. If the point that is being made that we have effects of the host of pollutants together from similar sources (for example, summer haze), then this

is OK. But in most settings it still makes sense to speak of effects being due to PM or SO_2.

6-238 Line 26-27. The "best" lag approach again.

6-256 The case-crossover study is first introduced here, but should be included in the intoduction to study designs on p.6-3.

6-258 Line 27. I think "mortality" should be "morbidity".

6-266 Line 17. This is a misuse of "strong" in this setting. These are all weak associations. The associations may be consistent, coherent, and have large public health impacts, but they are nevertheless relatively weak associations.

Chapter 8. Toxicology.

In general, this chapter does an excellent job of presenting a great deal of new, and often apparently conflicting, data. The summaries, especially the final summary, is well-reasoned and balanced, and makes conclusions with appropriate qualifiers.

As noted below, one important purpose of the toxicological work is to enhance the plausibility of the epidemiological findings. Much of the work done using easily studied particles such as ROFA, and work using extremely high concentrations of particles, although arguably useful when negative findings are obtained, are less relevant when attempting to interpret positive findings. This strongly motivates the use of CAPs studies where real-world particles are used. It is argued that because of day-to-day variability in the particle composition of CAPs, that experimental studies will not have the statistical power to use a factor analysis to successfully identify the components of CAPs that are particularly toxic. If valid, this would limit the usefulness of CAPS. However, recent work by Koutrakis's group (EHP 2000, see comments by Koutrakis on this chapter) in which factor analysis was successfully used for this purpose suggests that this is not the case. Although the findings from the multitude of toxicological studies are difficult to interpret, they have contributed to enhancing the plausibility of the epidemiological findings. It is anticipated, especially with further work using CAPs, that the picture will become clearer as work progresses.

Introduction

8-3 I like the notion of enhancing biological plausibility, rather than assessing dose-response, at this stage.

Respiratory effects

8-20 The paragraphs beginning on line 11, as well as those on 8-37 and 8-43, present useful perspectives on ROFA. The later discussion on the differences between tracheal instillation and inhalational exposures is also helpful.

Systemic effects

8-31 Line 27. Why does an increase in t-alternans suggest an anti-arrhythmic effect of PM?

8-34 This summary in para 1 is excellent.

Compromised

8-41 What is the paragraph starting on line18 doing here? There seems little place for the reference to the Nel paper, since the statement attributed to it (the increase in allergic rhinitis being due to diesel exhaust) is pure conjecture, unless it serves as a starting point to present findings to support or refute it, which it does not.

8-43 The paragraph starting on line16 on the Goldsmith paper is repetition of a previous paragraph on 8-37.

Mechanisms

8-65 Line 28. Need to justify the significance of alkaline phosphatase production, particularly since it seems, based on the preceding sentences, that silicon dioxide was potent.

8-68 The section on ultrafines beginning here presents an artificial motivation for interest in ultrafines. Yes, surface area will increase dramatically as particle size decreases, for a

given mass, as demonstrated in Table 8-9. However, it is clear, given the distributions of particle mass, particle surface area and particle number by particle size in ambient air, that particle mass falls dramatically as one enters the ultrafine size range: so much so, in fact, that surface area begins to fall before getting down to the ultrafine range, and then falls dramatically once the ultrafine range is reached (as shown in the Whitby plot on p.2-7, Fig. 2-1). I would drop Table 8-9. It is conceivable that the Whitby plot is outdated, since it is at least 23 years old. It might be useful to have similar work repeated for modern-day atmospheres.

8-82 The first paragraph describes a clinical study that has no place here. One could alternatively note that, "Clinical studies have observed....". Here is what the toxicological studies show:.....

Summary
This summary, as I noted above, is excellent.

Chapter 9. Integrative synthesis.

I would recommend that this chapter, as the title suggests, serve the primary purpose of an integrative synthesis rather than a stand-alone summary of the CD. Of course it is possible for it to partially serve as a summary, while still serving primarily as a synthesis, but this would take considerable thoughtfulness.

In terms of organization, I would like to see the chapter focus on the big issues that were largely unresolved at the time of the 1996 CD, and then proceed to addressing how much progress has been made in answering these questions. This should take the form of integrating new findings across discipline. For example, in addressing the issue of coarse fraction effects, the epidemiological findings in isolation would suggest that there are effects of the coarse fraction, apart from those due to the fine fraction, and that strong consideration should be given to setting a coarse particle standard of some form. However, this course is tempered somewhat when information on coarse PM measurement issues and exposures are also considered.

The chapter could end with posing questions that remain unanswered, and which still need further work.

Barbara Zielinska, PhD

Chapter 2: Physics, Chemistry, and Measurement of Particulate Matter

In my opinion, this chapter requires more work. At present, the chapter makes the impression on the reader that it was written by several independent authors, without any attempt to integrate it into one consistent document. Following are the specific examples:

1. On page 2-47, line 19-21 (Section 2.2.3), the authors state discussing the experiments with two quartz fiber filters deployed in series in order to examine the artifacts connected with SVOC partitioning: "Unless the individual compounds are identified, the investigator does not know what to do with the loading value on the second filter (i.e. to add or subtract from the first filter loading value)". I agree with this statement - moreover, even if the individual compounds were identified on back-up filter, the decision concerning adding or subtracting back-up filter loading would not be straightforward. However, the authors discuss subsequently in detail (page 2-51 to 2-62) in several places throughout the Section 2.2.3 several experiments with Teflon-quartz or quartz-quartz back-up filters that produced conflicting results. The references of Turpin et al., 2000, and Kirchsteller et al, 2000, are discussed on p. 2-52 – 2-53 and again on p. 2-61 – 2-62 (in addition, the reference of Turpin et al., 2000, is missing). This would be confusing to the reader who is not very familiar with the problem of positive and negative sampling artifacts. It would be desirable to organize the discussion in more consistent manner, shorten it significantly, and not scatter it throughout the whole Section 2.2.3

2. There are repetitions of the same statements throughout the chapter. For example, the discussion of sulfate and nitrate in western and eastern U.S. on page 2-21 (line 12-22) is repeated on page 2-51 (line 1-7).
3. The discussion of the various denuder techniques and their limitations (Sections 2.2.3.2 and 2.2.3.3) is certainly important, especially since the popularity of these techniques has increased greatly recently. The selection of the correct denuder type, its dimensions, flow rate, etc., greatly influence the results and incorrect conclusions could be drawn if the user is not familiar with the denuder technique. It would be desirable if authors put more emphasis on discussing these factors and organize them in more logical manner (instead of the extensive discussion of the front-back-up filters collection methods, which produce doubtful results anyway).

Some statements or opinions express by authors are not accurate, for example:

1. Page 2-19, line 18-19: "…some primary organic compounds … are found…in the fine particle mode." As a matter of fact, most of the combustion-generated organic compounds are found in the fine particle mode.
2. Page 2-24, line 13: "…adsorption of organic gases…(e.g. polycyclic aromatic hydrocarbons)". Only 2 ring PAH are gaseous at ambient temperature, with 3 and 4 ring PAH distributed between the gas- and particle-phases.
3. Page 2-53, line 3-12: this discussion is impossible to follow, is there part of the sentence missing?
4. The PC-BOSS and RAMS denuders are discussed extensively throughout the chapter (page 2-55, 2-58, 2-89, 2-103, 2-105). However, both devices use a virtual impactor upstream of the denuder that removes not only a majority of the gases from the aerosol flow, but also particles smaller than 0.1 um. Thus, the gas-particle distribution is changed even before the aerosol enters the denuder! In addition, particulate OC estimates have to be corrected for particle losses in the inlet of 46 to 48%. Is this 46 to 48% factor independent of temperature, pressure and other factors? How accurate are the measurements, taking into account these corrections? It would be desirable if authors discuss the limitations of these denuders as well as put the results obtained with these devices in proper perspective.
5. Page 2-95: The discussion of the commercially available automated carbon analyzer seems to be a little premature in this document, since no comparison data with other established techniques is available yet. There is no clear understanding what the instrument really measures in comparison with TOR and TOT techniques.
6. For completeness, a newly developed continuous photoacoustic technique for black carbon measurement should be included in Section 2.2.5. The technique and its applications are described by Moosmuller et al. (1998) and Arnott et al. (1999; 2000).
7. Page 2-103, line 18-23: One has to be careful when expressing the opinion that the denuder technique is an improvement over the filter/adsorbent collection method. It should be followed by the caveat that this is not an "out of the shelf" technique, it is not straightforward and requires thorough understanding by the user. If not used properly, it is subject to numerous artifacts and may lead to erroneous conclusions. Also, one doesn't have to use a charcoal impregnated glass-fiber filter for SVOC collection (especially that it is not readily available commercially); other solid adsorbents (such as PUF/XAD plugs) are used as well.

The minor problems that require corrections are as follows:

1. Page 2-10, line 4-5: missing word, "the term ultrafine", "the term nanoparticle"
2. Page 2-13, line 13: prior to 1987
3. Page 2-20, line 22: "…or on or in.."?
4. Page 2-21, line 7: "in" before SO4 not necessary
5. Page 2-25, line 1: "are" is missing
6. Page 2-33, line 29: what is "PNA organic compounds"?
7. Page 2-56, line 19-21: an awkward sentence, instead of which method?

8. Page 2-57, line 23-25: this sentence is a repetition of the line 16-17
9. Page 2-62, line 15: absorbent?
10. Page 2-73, line 19: The instrument operated by the Desert Research Institute was not a "high-volume carbon sampler", but the medium-volume (113 L/min flow rate) fine particles ($PM_{2.5}$) and semi-volatile organic compounds (i.e. filter followed by a solid adsorbent) sampler.
11. Page 2-77, line 13-14: an awkward sentence, I'm not sure what it means
12. Page 2-83, line 21-27: either "it is important" or "its importance"
13. Page 2-91, line 8: remove "because"
14. Page 2-105, line 23-25: not all ATOFMS instrument can measure particles ranging in size from 10 nm to 2 um (see page 2-94).

There are several missing references, mostly recent ones (Turpin et al., 2000; Casimiro et al., 2001) but also older, such as Turpin et al., 1991. I didn't check them all – it would be desirable if authors make sure that the references are in order.

References:
Arnott et al., 1999: Atmospheric Environment, 33, 2845-2852;
Arnott et al., 2000: Rev. Sci. Instrum., 71, 4545-4552;
Moosmüller et al., 1998: J. Geophys. Res., 103, 28,149 – 28,157.

Chapter 3: Concentrations, Sources, and Emissions of Atmospheric Particulate Matter
I would recommend several minor revisions for this chapter, as follows:

1. Page 3-5, line 1-3: Figure 3-2 shows that although the nationwide PM_{10} concentration trend shows the clear decline from 1989 to 1995, it seems to level-out for the last 3 years, especially for urban-suburban sites.
2. Page 3-6, Figure 3-3 is not clear. The reader may have troubles with assigning the EPA regions to the graphs.
3. Page 3-22, line 4: the main reason of heated inlets in continuous PM mass measurement instruments is to remove water (as discussed in Chapter 2), so the removal of water is not a sampling artifact.
4. Page 3-26, line 26-30, the discussion of Table 3-3: it is not apparent from the data presented in this table that water and cations associated with sulfate are the most abundant species in Philadelphia. Also, sulfate concentrations is not listed, just the total sulfur.
5. Page 3-28, line 7-9: not only trace metals concentrations are highly uncertain; Al shows very high uncertainty as well.
6. Page 3-30, line 18 to the end of the paragraph, the discussion of Table 3-5. The selection of marker species for individual source categories seems to influence greatly the results. In particular, Pb, Br and Mn as the only tracers do not seem to adequately represent motor vehicle emissions.
7. Page 3-35, Table 3-7: EC sources for anthropogenic PM>2.5 include tire and asphalt wear as well.
8. Page 3-42, line 13-15. Table 3-1 doesn't show that water, sulfate and cations associated with sulfate are the major components of PM in the eastern U.S. Also, the newer studies listed in Table 3-8 showed that not only diesel but also gasoline vehicle exhausts are important sources of PM.
9. Page 3-45, line 8-10: an awkward sentence
10. Page 3-45, line 30: 1998, not 1988
11. Page 3-46, line 5-6: "However… but…"?
12. Figure 3-23, page 3-50: the figure caption says "… principal source categories for nonfugitive dust sources…", but the figure shows 44.2% of fugitive dust contribution.
13. Page 3-56, line 11-13: This is not a valid argument, since $PM_{2.5}$ which are discussed here, have longer residence time.
14. Page 3-56, line 28-30: an awkward sentence

15. Page 3-57 and 3-58, line 29-31 and 1-3: please clarify
16. Page 3-59, line 7-9: the discussion on page 3-55 and 3-56 states that the reasons for this apparent discrepancy between emission inventory and receptor modeling results are not clear.
17. Page 3-59, line 21: what PM2.5PM10 refers to?
18. Appendix 3A: Table 3A-2 should include some data from more recent Northern Front Range Air Quality Study (NFRAQS), carried out in winter 1997. Ambient data are presented in volume A (Chow et al., 1998) of the final report (Watson et al., 1998) and are available on the web (http://www.nfraqs.colostate.edu/index2.html)
19. Appendix 3A, Table 3A-2: Are organic compound concentrations really in ngC/m^3 (C = carbon) or rather in ng/m^3?
20. Appendix 3B, page 3B-12, line 13-15: fuel type?
21. Page 3B-13, line 1-10: are "diesels" mentioned here light- or heavy-duty vehicles?
22. Page 3B-18, line 1-17: PAH were also reported in volume B (Zielinska et al., 1998) of the NFRAQS final report (Watson et al., 1998)
23. Page 3B-18, line 7-10: at atmospheric conditions, PAH with mw 228 (BaA, chrysene and triphenylene) are predominantly particle-associated, with only traces of these PAH in the gas-phase (see, for example, Arey et al., 1987).

References:
Arey et al., 1987: Atmospheric Environment, 21, 1437-1444 (page 1439)

Joe L. Mauderly, DVM

Chapter 7: Dosimetry of Particulate Matter - General Comments:
This chapter covers a reasonable range of topics, but needs some editing. There are several places where terms are used incorrectly, or where uncommon terms are not defined.

Throughout the chapter, it should be stated whether the exposures of humans were nasal, oral, or both. The difference affects deposition, as the author notes, and the results from individual studies can't be placed in context by the reader without the information.

Throughout the chapter, it should be stated whether the models and their predictions have been validated by comparison of results to those from actual measurements. More models have not been validated than have. This is an important point for the reader to understand.

The chapter could benefit from the addition of a few more figures and tables showing comparative data that illustrate the points being made. A reader well-informed on deposition/retention issues can understand the points being made, but many readers will have difficulty envisioning the relationships described. A simple graph of particle size vs. regional and total deposition taken from any of the several sources cited would help. Figure 7-1 is not inappropriate, but it falls unnecessarily short of illustrating both total and regional deposition. A table listing some representative values for comparative (between species) amounts of deposited and retained PM of a few discrete sizes would also help. Other than the figure on Page 7-8 and the flurry on pages 7-30-31, the chapter makes no use of tabular or visual material to illustrate key points.

Specific comments:
P 7-3, L 12: Don't confuse "aerosols" with "particles". It's the particles that have a polydisperse size distribution. The "size" of an aerosol is the size of its container.

P 7-6, L 1: All deposition is "by physical contact". What we are talking about are the mechanisms that cause physical contact. A material is deposited when contact is made, regardless of the cause.

P 7- 6, L 15: Are particles charged either negatively or positively? If so, are there charges that reduce deposition as well as those that enhance it?

P 7- 7, L 10: By definition, if a particle is in the "inspired volume" it is inhalable. Conversely, if a particle is not inhalable, it won't be in the inspired volume. This sentence should read "—particle present in the ambient air".

P 7-9, L 1-13: For these citations, state whether the exposure is nasal, oral, or both. That makes a big difference for ultrafines, and the smaller the particle, the greater difference it makes.

P 7- 14, L 24 – P 7-15, L 3: You need to state that these are estimates from models, not actual measurements, and you also need to state the type of model used.

P 7-15, L 11-12: The sentence implies that there geographical areas where coarse PM are <u>not</u> present. Where would such an area be?

P 7-15, L 29: Again, do not use the word "aerosol" for "particle".

P 7- L 17: Once again, it's "particle" not "aerosol".

P 7-19, L 5: Give the geometric standard deviation for the ROFA.

P 7-19, L 18: Throughout the chapter, you should state whether the exposures were nasal, oral, or both. This is an important variable, and deposition really can't be understood without this information.

P 7- 22, L 3: This study measured total deposition, not "lung" deposition.

P 7- 22, L: It is not clear how a tumor would increase diffusion deposition.

P 7-24, L 13: It is not clear what the "shallow region of the lungs" would be. Would this be the central airways?

P 7-25, L 14: Of course inhalability can be important for humans. It's important in a dust storm. It's important if you are riding a motorcycle (remember the old joke about bugs in the teeth).

P 7-25, L 25-26: What does "upper and lower airway bifurcations" mean?

P 7-26, L 6-7: Just say "—generation is constant" rather than "adopts a constant value". It's hard to see how an airway generation can adopt anything.

P 7- 26, L 14-20: A figure would help the reader understand what you are saying about deposition minima and maxima. A simple line graph showing fractional deposition with particle size for humans and rats, for example, would be useful.

P 7- 27, L 9: Mention whether or not these model predictions have been validated.

P 7- L 14: First, it's the MMAD of the particle size distribution, not the "aerosol" distribution. Second, give the geometric standard deviation of the size distribution.

P 7- 27, L 15: What does "comparable respiratory intensity levels" mean? I don't know what "intensity level" might imply.

P 7- 27, L 22: Again, has there been any validation? It is important throughout the chapter to indicate whether or not models have been validated against actual measurements.

P 7-28, L 9: The statement is incorrect. The study did not measure the "volume density of deposition", whatever that might be. The study measured, using a morphometric technique based on volume density, the retained material. A post hoc study of tissue cannot evaluate deposition, but only the amount and location of retained material.

P 7- 28, L 12-14: The statement is incorrect. It is not true that "different cells contact retained particles" in the two species. The difference was not absolute. There was relatively more material in the interstitium in one species and relatively more in the alveolar lumen in the other, but there was some material in both compartments in both species.

P 7- 28, L 21: The point is that there can be greater differences between abnormal humans and normal rats. The present wording doesn't convey this; it suggests that the greater difference you are talking about is between humans and rats.

P 7-28, L 23-27: This section inappropriately brings response into the dosimetric picture. Dose is dose regardless of response – these are related, but separate, issues. Interspecies dose extrapolation per se has nothing to do with interspecies differences in response or dose-response relationships. Comparative response has to do with both differences in both dose and response, but comparative dose has nothing to do with differences in response.

P 7.29, L 3: In summary, this section could greatly benefit from some tables or figures showing example results and comparisons. It also needs attention to which model predictions have been validated.

P 7-32, L 23-24: The magnitude of response also has to do with PM composition, not just with particle number.

P 7- 33, L 1-11: Lymphatics should be mentioned in this paragraph.

P 7- 33, L 14: Do you mean 5% by mass or number?

P 7- 33, L 17-18: Alveolar surface fluid is also transported, at least in some in part, up the airways. Surfactant of alveolar origin has been reported in the surface fluid of conducting airways. If this is true, then you should mention this path rather than implying that all PM-derived material solubilized in alveolar fluid is absorbed through the epithelium.

P 7-34, L 8: What do you mean by "nonuniform"? Do you mean spatially or temporally non-uniform within individuals, or are you referring to variability among individuals?

P 7- 35, L 5: You need to clarify throughout this chapter whether the statements about deposition site are derived from measurements or whether these are assumptions from deposition models. Most, if not all, are from the latter, which assume plug flows that are not likely to be absolute.

P 7-35, L 22: Deposition was "estimated", not "calculated". The latter term implies a certainty, or direct measurement, that doesn't exist here.

P 7-37, L 25-26: The phagocytic activity need not necessarily be decreased, it could be simply overwhelmed. More particles could reach the interstitium because of either or both effects.

P 7- 40, L 18: You need to explain what "mechanisms such as two-phase gas-liquid interaction" means.

P 7- 40, L 20: Do you mean that transport is more effective (ie, more rapid)?

P 7-41, L 13: It should read "—those obtained".

P 7- 41, L 21: I doubt this statement. I'd wager that more coughs occur in the U.S. annually because of internal reasons (viral infections, chronic bronchitis, etc.) than from an "inhaled stimulus".

P 7- 42, L 29: Again, there is confusion between deposition and retention. The 1 mg value is an amount of retained PM, not deposited PM. If you deposit that amount slowly enough, there will be no overload from the deposition.

P 7- 44, L 16: Do you really mean "random" here, or do you mean "uniform"? I think the latter would be a better term.

P 7-46, L 18: It should read "The model results were in good agreement", not that the "model" was in good agreement. "Models" don't agree with anything, but good ones produce "results" that do.

P 7- 47, L 7: Any results or validation here?

P 7- 47, L 15: Again, any validation?

P 7- 47, L 27: Once again, any validation?

P 7- 47, L 29: Please explain what "general dynamic equation for size evolution" is. I don't understand this, and there may be others like me.

P 7- 48, L 9-10: I think you are saying that the combined effects yield a narrower size distribution. If so, why not just say that, instead of saying "decrease the size nonuniformity" and "variance"?

P 7-50, L 16: It should read "—data are". Data is a plural word.

P 7-50, L 21: Define "acinar airways". That's a new term for this chapter.

P 7- 52, L 25: It should read "—rats and monkeys exposed—". The statement talks about two species, but you only name one.

Chapter 8: Toxicology of Particulate Matter - General Comments:

The chapter is a good draft, but needs considerable editorial clean-up of both text and tables, and some additional attention to content and conclusions. The former is addressed by numerous of the following specific comments. The latter pertains to the several places where sentences that portray conclusions (although not necessarily marked as such) that are unclear, misleading, or in conflict with one another. These are also addressed in the specific comments below.

The chapter could be better balanced in its treatment of the types of PM that are emphasized. As one example, it contains greater emphasis on ROFA than is warranted. Granted, there has been a tremendous investment in ROFA research, but aside from demonstrating the importance of soluble transition metals (which is important), the extension of this work to other ambient PM is limited. As one contrast, very little attention is given to "bioaerosols", and what information

there is pertains almost solely to endotoxin. As another example, no convincing rationale is given for excluding the considerable database from engine emissions studies from this chapter. Diesel PM is cited for its potential adjuvant effects, but no mention is made of the several other potential effects of either diesel or other combustion PM and co-pollutants. Therein lies our greatest body of information on PM and co-pollutants, and some studies have explored the absolute and relative roles of different constituents of the mixture. It is especially astonishing that, while the emissions studies are ignored, studies of animals housed in urban and rural air, with no characterization of exposure, are cited. The latter have provided almost no useful information to date on the additive or interactive effects of PM and co-pollutants.

Regarding endotoxin, it is noted in one paragraph that ambient particles may have been contaminated by endotoxin – presumably during handling and storage. If this is a concern, and it may certainly be, why not note the concern more broadly with regard to many, if indeed not all, of the studies using collected particles? This surely is not a concern only for those studies to which endotoxin effects are central.

The exposures cited in the text (and in some cases, in the tables) need to be more uniformly and more completely described. There are numerous instances in which studies are cited for which either the PM exposure concentration, time, or pattern are not given. Noting an effect, for example, of an exposure and only listing the concentration does not give the reader adequate information to place the findings in context.

The text and tables need to be screened to ensure that all abbreviations are defined. Some are apparently not defined.

The discussion of ultrafine particles seems to be ignorant of the portion of ambient ultrafine PM population that is in droplet, rather than solid, form. The discussion follows the classical ultrafine litany of greater penetration and surface per unit mass, but never mentions the ultrafine particles that are likely to spread, disperse, or dissolve after contact with liquid surface layers, and thus are probably never apparent to cells as "particles" per se. The points to be made are: 1) an acknowledgement that such PM exist, are ubiquitous, and need to be studied; and 2) there has been little or no research on this class of material.

Finally, the chapter does not do an adequate job of summarizing the key changes in our understanding of the toxicity between this and the last PM Criteria Document. The last section gets at this issue, but needs to be bolstered. As just one example, the Mechanisms of Action section (8.7.2) is a single paragraph that states that there may be more than one mechanism and that we don't know the mechanisms "unequivocally". While those are both true and understatements, there is not an indication of whether we know more about the plausbility of any mechanisms (ie, have more evidence) than we did last time. We do.

Specific Comments:
P 8-1, L 15: It should read "ambient PM", not "ambient air".

P 8-2, L 23: It is not clear what "total" means in "total exposure".

P 8-3, L 4-5: The distinction here is not clear. Presumably, both "low" and "high" toxicity PM cause effects because of size and composition. Are PM of low toxicity neither ambient or surrogate?

P 8-3, L 8-11: The selective treatment of diesel particles (DPM) is not clear and is of questionable logic. DPM can cause a range of non-cancer effects. They are an integral component of PM nearly everywhere, and can predominate in some microenvironments. The fact that EPA developed a separate hazard assessment for diesel emissions should not preclude the inclusion of DPM in this document. The selection of only the potential immunological

effects of DPM for discussion in this document doesn't seem logical. At a minimum, this document should summarize the conclusions from the diesel hazard assessment.

P 8-3, L 14-16: There is something wrong with this sentence. First, it seems to mix the issues of inhalation and instillation. Second, it probably isn't true that most studies have used inhalation. Probably more have used instillation. The points that 1) both methods have been used, and 2) most doses have been high, are valid, but the sentence is confusing.

P 8-4, L 5-14: This paragraph needs attention. First, the only study in healthy volunteers in Table 8-1 uses a concentration of 1000 :g/m^3, yet the text notes 2000 :g/m^3. Second, the text discusses clearance, but there is no report in the table about clearance. Third, if you are going to cite studies or results in the text that are not in the table, give the references.

P 8-4, L 17: If this is a 1997 reference, why isn't it in the table?

P 8-5, Table 8-1: First, give the exposure days/wk for the studies (first two) that use repeated exposures. Second, if the first study used only neutral sulfites, why is it in an "acid" table? Third, shouldn't the units in the Lee study be :g/m^3 and not mg/m^3?

P 8-6, L 9: How do you get "up to 6400" mg/m^3 if the exposures were for either 100 or 200 mg/m^3 for 45 min, as listed in Table 8-2?

P 8-6, L 22: References for the first statement?

P 8-6, L 25: Was it the vanadium or the responses that were elevated 9-fold? How do we know that the effects were due to vanadium in these subjects?

P 8-7, Table 8-2: For the Lay et al. Studies, why not give mass doses like the rest of the listings in the table? Did the paper not report mass doses (I think it did).

P 8-8, Table 8-2: In the last listing, was all of the ROFA vanadium pentoxide? Shouldn't the "particle" listing be ROFA?

P 8-9, L 13: It is not clear what a "host generated decrease in the availability –" means. Does this mean that reactive iron was removed after deposition?

P 8-11, Table 8-3: First, why list the concentrator type for the first study if you don't for the rest of the CAPS studies? Second, "CAPS" is not a sufficient descriptor. The location and time of concentration (at least something like "Boston, fall 1999") should be given. This document should avoid perpetuating the common, but naïve, notion that CAPS is some standardized or consistent material. Third, the age of the subjects is given for some studies and not others. If age is important (and it probably is), it should be given for all. The same for gender. Fourth, for the Kennedy et al. Study, give the dose administered. Fifth, what is the distinction between "instillation" in the Kodavanti et al. Study and "intratracheal instillation" in the Li et al. study? Finally, how could "instillation" in the Kodavanti et al. study be administered "6 hr/day – 2-3 days"?

P 8-13, Table 8-4: First, in the Brain et al. study, the time and location of sample collection should be in the "Particle" column, not the "Size" column. Second, the age and gender of the subjects should be listed. Third, where are "CFA, CMP, WC, and MCT" defined (Broeckaert et al. study, Costa & Dreher study)? Fourth, what does "emission source" mean in the Costa & Dreher study? What emission, what source? Fifth, in the Gardner et al. study, why note that the material was instilled in saline? Does this mean that none of the other studies used saline as the vehicle if it wasn't listed? Are the "0.3 and 1.7" ml, mg, or what? Sixth, why is "exposure duration" listed as "N/A" for the Gavett et al. study. "Duration" is given for other instillation

studies, and is presented as observation time after instillation. Seventh, no PM size is listed for the Hamada study. Eighth, what word is "alveotis" supposed to be in the description of the Kodavanti et al. 2000b study? Finally, were the deposited doses the same for instillation and inhalation in the Watkinson et al. study?

P 8-18, Table 8-5: First, give age and gender of subjects for each study. Second, in the Creutzenberg et al. study, does "retention increased" mean that clearance slowed, or simply that the lung burden increased? If that is the only reported effect, why bother to list the study?

P 8-19, L 1010: What were the lengths of the exposures cited in the paragraph. As a general principal, exposures need to be described by concentration, pattern, and length in order to be placed in context by the reader. Concentration alone isn't an adequate description of an exposure.

P 8-23, L 7: If by "injected" you mean instilled, then use "instilled" as is done elsewhere.

P 8-23, L 19: The important issue is not whether biologicals can "account" for the PM effects, the important issue is whether they might contribute to the effects. It's not a credible proposition that any single PM feature or type can "account" for the effects.

P 8-24, Table 8-6: First, if the PM concentration and size aren't known in the Cormier et al. study, and the only particle description is "swine building", what is the study doing in the table? We apparently have no idea what the exposure was or what part particles might have played in the effects. Second, in the Elder et al. study, does the 100 : g/m^3 refer to the carbon, the endotoxin, or both? Third, was there no estimate of PM concentration in the Rose et al. study? Overall, the poor characterization of exposures in the studies in this table renders most of them pretty useless for understanding the respiratory effects of bioaerosols. Aren't there any reports of effects of airborne pollen? Those are also bioaerosols.

P 8-26, Table 8-7: First, are "OTT" "MSH" defined somewhere? Second, why give the monocrotaline dose in the Costa & Dreher study – that isn't given for other monocrotaline references. Third, the location & time of collection of the CAPs should be given. Fourth, is "FOFA" something different than "ROFA"? Fourth, the gender & age of subjects should be given. Finally, the Minami et al. paper is a ridiculous citation. Both the experimental design and the interpretation are absurd. They injected undefined material into the jugular vein until the animals died, and noted that the heart acted up before death. You could do the same with tap water! This is an excellent example of the fact that not all published papers are worth including in this document. You can publish almost anything, but that doesn't mean that all publications contain meaningful information.

P 8-29, L 6: Here and elsewhere, the author's name is "Muggenburg", not "Muggenberg".

P 8-31, L 15-19: It is noted that there was little pulmonary effect in the dogs, but also that lavage neutrophils were doubled. That apparent conflict needs more explanation.

P 31, L 21: "Indice" should be "index".

P 8-31, L 26: "Suggests" should be "suggested".

P 8-31, L 26-28: This sentence doesn't make sense. Why do you call an increase in T-wave alternans an "anti-arrhythmic" effect?

P 8-32, L 6-19: This paragraph is confusing, and suggests that the author must be confused about these dog studies. It notes that Muggenberg (sic) found results in dogs exposed to ROFA that contrast with Godleski's results in dogs exposed to CAPs. That's an "apples and oranges"

comparison. Later, it notes that the Muggenburg ROFA was collected at a different time than that used by Godleski, but never cites any Godleski ROFA study. What happened was the Godleski did studies with ROFA, then proceeded to work with CAPs. Muggenburg did studies with ROFA provided by Godleski, got different results than Godleski's ROFA results, and then found that the ROFA provided by Godleski wasn't the same as Godleski had used before. There isn't any connection between the ROFA studies and the CAPs studies. The point that the findings of little (Godleski) or no (Muggenburg) effect of ROFA suggests that the typically small amount of metals in CAPs may not be driving the effects of CAPs has some validity. In order to make that point, however, you need to clean up the paragraph.

The fact that different animal studies yielded different results doesn't reflect the problem of interspecies extrapolation, as stated. It reflects the difficulty of extrapolating among any differently-designed studies (animal or human). The animal studies quoted did not use the same exposure materials, and the results differed. That's understandable, but doesn't have much to do with interspecies extrapolation.

P 8-34, L 4-14: Another hypothesis that is not mentioned here is the direct transfer of PM from the lung to the heart. That has been shown to occur, although it's poorly documented and understood.

P 8-34, L 20: Has an effect of nutritional status on individual susceptibility to PM been demonstrated? If so, cite a reference. If not, don't imply that it has.

P 8-36, L 27-28: The difference in rat responses between the labs is more likely due to the difference in CAPs than to differences between rats or labs. This possibility is not even mentioned. As in other places, the wording here suggests the very naïve view that "CAPs is CAPs". You can hardly calibrate one response against another unless you show that the exposure material was identical.

P 8-37, L 7-8: I guess it depends on what you call a "limited number". There have been quite a few real-time exposures to CAPs now, and several to actual urban air.

P 8-37, L 15: I think you mean "no difference in lung volumes" rather than "no difference in lung volume measurements". The two are not the same.

P 8-38, L 20: "Organisms" should be "mice".

P 8-40, L 5: What kind of particles were acid coated?

P 8-40, L 15: The two "loci" should be "locus".

P 8-40, L 27: Why note that "replication of this study is necessary"? Why any more necessary for this particular study than for others?

P 8-42, L 13: Greater than additive to what, or in comparison to what?

P 8-43, L 18: This sentence says "daily exposure", but the preceding sentence says "single exposure". What kind of exposure are you really talking about?

P 8-45, L 14-15: How do the two quoted studies of BAL show that DPM cause an increased antigenic response in the nose?

P8-46, L 1: "Antimicrobial defenses against microbes" is redundant.

P 8- 46, L 16: What exposure level of DPM?

P 8-47, L 23-27: These two sentences are redundant.

P 8-48, L 10: There ought to be a paragraph in this section, perhaps here at the end, describing the different cell types used in the in vitro studies, and their relevance to cells in the human respiratory tract.

P 8-55, L 24-29: The point is made here that endotoxin might be a confounding factor in the response to ambient PM. It is good to note that endotoxin might be an important factor in some ambient PM. On the other hand, if there is concern that endotoxin contamination after the fact might have confounded this study, why would the same concern not be expressed for every other study that used collected and stored samples of not only ambient, but also other types of PM?

P 8-60, L 24: "Correlated" should be "correlate".

P8-62, L 3: Do you really mean a "combination of several components" as the sentence says, or do you mean a combination of metals? The subsequent sentence continues talking about multiple metals. "Components" includes both metals and lots of other constituents.

P 8-62, L 12-13: The statement suggests that all biological responses of ambient PM and ROFA depend on metals. Certainly, metals have been shown to play a key role in some responses, but you surely don't mean to imply that metals are the key to all biological responses to all PM.

P 8- 62, L 16-17: It should be "hours" and "sides".

P 8- 63, L 9-10: The last statement in the paragraph is correct, but the paragraph only deals with metals. The section is on reactive oxygen species. The material in the section tends to leave the reader with two false impressions: 1) that all reactive oxygen species are mediated by metals, and 2) all biological effects are due to metals, and by extension, to reactive oxygen species. Do you really intend to make these claims? If not, the paragraph ought to mention mediation of reactive oxygen species by other PM constituents, and make clear that you don't intend to imply that all biological effects are caused by this pathway.

P 8-70, L 23: "Time" should be "times".

P 8-71, L 5-7: There is evidence to support this statement for slowly-soluble, solid ultrafine particles, but that is only a part of the ultrafine PM population. This statement, like the entire section, seems to be ignorant of the existence of the portion of ultrafine PM that is not solid, but consists of droplets, mostly organic material and often condensed on nuclei of sulfur compounds. For example, this type of material makes up a sizable portion of the number count of ultrafine particles in engine emissions. To the extent that these particles are miscible in the liquid layer covering the epithelium, they would cease to exist as "particles" per se, and would not penetrate cells as such. While it is true that there has been almost no research on this class of PM, it is also true that we know it exists, and can't be ignored in the CD.

P 8-77, L 20-21: The type and ratios of pollutants are key factors that are missing from this recitation of factors affecting interactions.

P 8-78-79, Table 8-10: This table and the text seem to ignore the most common studies of combined PM-gas mixtures, studies of whole combustion emissions. Emissions studies are all studies of PM and co-pollutants, and several have tested the importance of different components. It is inappropriate to only cite studies of simple combinations of two or a few components and ignore studies of complex mixtures.

P 8-80, L 18: Again, what about the many emissions studies?. It is not true that the toxicology database is quite sparse in this regard.

P 8-81, L 9: "Interaction" should be "interactions".

P 8-82, L 16 to P 8-83, L 8: It is astonishing that these field studies of whole air (urban and otherwise) are cited as contributing to our understanding of the co-pollutant issue, while well-characterized combustion emission studies are not cited at all! These studies provide very little useful information. With regard to the topic of the section, they are basically ecological epidemiology studies with very few subjects of the wrong species. In line 26-27, it is stated that "extrapolation is hampered" by a lack of exposure characterization. What an understatement! Considering all the problems with these studies, it is questionable whether they merit inclusion at all. As in all air pollution studies, but especially true for studies of co-pollutant interactions, if you don't know the exposure, you don't know anything.

P 8-83, L 21-22: I disagree with this statement. The key to plausibility is not knowing the components and the individuals at risk. The key is to plausibility is understanding the linkage between the two (ie, a plausible mechanism).

P 8-85, L 13-14: This sentence contrasts with the earlier statement on page 8-63 that metals have been established as a key (it actually implied metals were the only key) contributor to health impacts of PM via reactive oxygen species. It is stated that the ROFA studies have important implications, but it doesn't state what the implications are.

P 8-86, L 5-14: This section on "bioaerosols" only talks about endotoxin. What about all the other bioaerosols? Endotoxin is seldom, if ever, actually a "bioaerosol". It is a contaminant of airborne PM. Pollen proteins, plant debris, and many other airborne materials of biological origin are not mentioned.

P 8-86, L 20: First, "PM is responsible" should be PM are the responsible". Second, there other health effects of concern for diesel PM in addition to the adjuvant effect. Why not mention them in this chapter?

8-87, L 29: It should say "animals with certain types of compromised health", or "animals with compromised cardiorespiratory health" or some such wording. Not all types of compromised health would be expected to affect susceptibility to inhaled PM (a broken toe, as an extreme, but illustrative example).

P 8-88, L 3-6: This closing statement needs work. First, validation of animal models is as important as identification, and this important point is overlooked in the section, and too often overlooked by researchers. Second, what is the connection between making "solid progress" and the fact that large numbers of people are needed for epidemiology studies? Would our progress be less solid if fewer numbers of people sufficed for epidemiologists? The author probably has a couple of good thoughts here, but it's not clear that they belong in the same sentence.

P 8-88, L 12-13: This sentence is trite. I think we can go beyond saying that there "may be" multiple mechanisms to state that research to date clearly indicates that there "are" multiple mechanisms.

Chapter 9 Integrative Synthesis - General Comments:
In general, the chapter is well-developed, and with some modest editing, will serve well as an integrated synthesis. With minor editing, it will hit approximately the right level of detail, and give appropriate attention to making the major points and drawing conclusions.

Some additional attention needs to be given to this chapter to accommodate the fact that many people will read only this chapter. It proposes to be a synthesis of all of the Criteria Document except the environmental effects. First, one wonders why the environmental effects couldn't

also be summarized. Second, the chapter needs some additional definitions, attention to terminology, and figures in order to better serve as a stand-alone summary.

There are inaccuracies in this chapter that carry over from the same problems in preceding chapters. There are also sentences scattered throughout the chapter that don't make sense as written. This may have resulted from attempts to condense more expanded information in preceding chapters, but it needs to be corrected.

Specific comments:
P 9-3, L 14-15: While it is true that the term "aerosol" is often used incorrectly, why not use the correct terminology in the CD? "Aerosol" and "particle" are not the same thing. This chapter perpetuates the error.

P 9-4, L 16-18: It is stated that the nuclei mode is only distinguishable in remote areas or near sources. Elsewhere, it is stated that the nuclei mode is not observed in remote areas. Because the nuclei mode is short-lived, it presumably would be found only near sources; thus, if it is in remote areas, there must be sources there. These facts need to be reconciled so the chapter presents a consistent story.

P 9-4, L 20-21: I have heard emission scientists distinguish "nanoparticles" as being in the 50 nm or less size range. Does the Agency care to set forth any criteria for these terms? That would be a useful service.

P 9-9, L 1 and 5: Wouldn't PM formed by condensation also be called "secondary"? That is, not all secondary PM is formed by "chemical reactions", right (or do you call condensation a chemical reaction)?

P 9-14, L 11-12: It is not clear if you are saying that these species exist, or should exist, or possibly exist, or what.

P 9-15, L 6: This statement conflicts with P 9-10, L 19-20 that states that nuclei mode particles are not found in rural areas. Let's settle on one story and stick to it.

P 9-15, L 28-29: The meaning of this sentence is not clear. The point about not being able to characterize particles because of lack of reference standards is not clear.

P 9-16, L 3: It should be "data ----<u>are</u> needed". Data is a plural word.

P 9-16, L 31: The point about particle-bound water is not clear. In fact, the whole issue of particle-bound water is not clear. Presumably, water is associated with some PM in the atmosphere. If so, then water is part of the particle, and you want to know the mass and number of particles, and their health effects, <u>with</u> water, not without. I can see how you would want to avoid data that include the accumulation of water by particles <u>after</u> collection, but why would you only want to know the mass of particles with <u>no</u> water?

P 9-18, L 1-2: It would provide useful perspective to give a typical portion of PM mass that cannot be speciated at present. It is often the majority of mass, not a tiny portion. That would be a surprise to most people.

P 9-20, L 3-4: State the time period of the children's health study, or the information here is not useful.

P 9-21, L 5-6: It is not clear what you mean by saying that the amplitude of the peaks is smaller than the daily means. That is not intuitive, and the reader (eg, me can't understand your statement.

P 9-24, L 4-5: It is not clear what you mean by "not influenced by exhaled breath" If exhaled breath actually influences the nature or concentration of materials in the breathing zone, then why would you exclude that effect? Another example of how you need a bit more explanation for this summary chapter.

P 9-26, L 8-24: This entire paragraph is difficult to follow. If the "attenuation factor" is worth mentioning (which I don't doubt), then you need to explain it and its application more clearly. It can't be understood from this section alone.

P 9-27, L 10-14: This information is repetitive of earlier sections.

P 9-31, L 6: It should be "breathe", not "breath".

P 9-32, L 4: Is should be "alveolar", not "alveoli".

P 9-32, L 9-13: These sentences repeat errors that were noted in Chapter 8. First, the study did not evaluate deposition at all. It evaluated the location of retained material, and that could differ from the deposition site. Second, it is not true that different cells were exposed in the two species. The site of predominant retention differed between the species, but there was overlap. The same cells were exposed - just to a different degree, or with a different prevalence, in the two species.

P 9-34, L 22: Where are the data supporting this statement? I don't know of data showing that "overload" affects clearance differently in rats and humans. You would have to measure clearance rates in rats and humans having the same degree of "overload", and that hasn't been done.

P 9-36, L 12: What is a "biomedical" coherence? Do you mean "biological"?

P 9-37, L 3: Ambient PM exposure is always, not "usually", accompanied by exposure to other pollutants. Why be tenuous about this?

P 9-43, L 2-3: This sentence is not clear. What is the point about "identifiable" PM episodes?

P 9-60, L 26: This is the first time I've heard PM charged with affecting "morality"! I think you mean "mortality".

P 9-66, L 23-29: First, this 7-line sentence need broken up. Second, what is meant by "semi-individual"? Third, eliminate "studies" in line 26.

P 9-70, L 4: It should be "admissions of persons".

P 9-72, L 22: It should be "there are some data".

P 9-73, L 13-17: The sentence is confusing. It appears as though you are saying that CO could be a better surrogate for PM than PM itself. If that's not what you are saying, what are you saying?

P 9-75, L 15: "Suffers" should be "sufferers".

P 9-75, L 18-24: This paragraph is not clear. It is especially not clear what you mean by the sentence on lines 23 and 24.

P 9-76, L 11: It should be "these data were".

P 9-76, L 30: It should be "these data".

P 9-77, Figure 9-11: The label of the horizontal axis should be "Change in Peak Flow", not "pulmonary function". Peak flow is what was measured, and that's only one of myriad indices of pulmonary function.

P 9-81, L 1: It should be "relation to season".

P 9-82, Figure 9-13: First, in this summary chapter, you need to explain "posterior distribution". Second, there is no value in the inset box in the upper right hand corner of the figure because the numbers are all the same. What's the point?

P 9-83, L 14-15: If the advance is so noteworthy, it is worth explaining in this summary chapter. From this chapter, the reader doesn't know what a "distributed lag model" might be. The chapter explains lags, but not distributed lag models.

P 9-84, L 13: Again, what are "posterior mean effects"? When you first talk about the "posterior" terms on earlier pages, you need to explain what you mean.

P 9-84, L 23: What are "secular" components? Are they defined in this chapter?

P 9-85, L 2: Again, you need to explain the attenuation factor. This parameter and its significance are not adequately described in the chapter.

P 9-85, L 12-14: It is not clear what you mean by saying that correlations are not correlated. The sentence needs re-writing.

P 9-85, L 24: "Statical" should be "statistical".

P 9-86, L 15: It should be "correlations".

P 9-87, L 29: Use the term "48 contiguous states", as you do later.

P 9-88, L 6-26: It would help make your points if you included example figures from the Krewski et al. paper. Unless the reader is familiar with the figures, it is hard to envision the points you are making from them.

P 9-89, L 8-11: This sentence is not clear.

P 9-89, L 14: "Materials" should be "information".

P 9-94, L 8: You should just state that the material was ROFA, instead of "combustion particles". You talk about ROFA elsewhere, and using a different term implies that this was something different.

P 9-95, L 1: The statement is incorrect. It is clear that particles enter the blood. There is lots of evidence for that, unless you envision transport to other organs via some other mechanism. What we don't know are the mechanisms and transport rates. We certainly know that transport occurs.

P 9-96, L 20-22: Perhaps this sentence was intended to start the next section. It doesn't belong where it is.

P 9-97, L 22: Gee, I thought the review draft diesel HAD was marked "do not cite or quote".

P 9-98, L 4-11: This section purports to refer to "bioaerosols", but like the bioaerosols section in Chapter *, it only refers to endotoxin. That's far too narrow a view of bioaerosols, and misleads a poorly-informed reader.

P 9- 98, L 13-20: The criticality of analyzing CAPs composition should be mentioned. Such studies place a premium on knowing composition, and are nearly useless without that information, yet CAPs studies often to not. This is an issue sufficiently important to mention.

P 9-98, L 22-31: It is not clear why this section is included under links between PM components and health. It is a related, but different subject, and warrants its own heading. In fact, it fits better under the next major heading.

P 9-101, L 26: Has "COH" been defined?

Allan Legge, PhD

OVERALL COMMENTS:

These comments are restricted to Chapter 1 Introduction and Chapter 4 Environmental Effects of Particulate Matter found in Volume I. The authors of Chapter 9 are to be commended for all of their efforts in revising this chapter. The text is significantly improved and expanded in important areas over the first draft of October,1999. Much more effort has been made by the authors to tell the readers what the science 'says'. This will greatly help in the 'risk assessment' analysis from the welfare perspective. One very important point emerges a number of times in the text and that is that welfare responses are very much driven by the history of exposure of the various environmental receptors. While there is some repetition of material in the text, it does not distract the reader.

SPECIFIC COMMENTS:

A. Chapter I. Introduction

1. Page 1-2,line 11. '—sulfate' should read '—sulfur'.

B. Chapter 4. Environmental Effects of Particulate Matter.

1. Page 4-4,line 4. The term 'runoff' should be replaced by 'washoff'.
2. Page 4-5,line 17. Should read "Neither nitrate nor sulfate".
3. Pages 4-6 and 4-7,Section 4.2.1.1 Effects of Coarse Particles.

The issue of 'saline aerosol' due to either road salt or cooling tower drift is missing from this section. The following references are suggested:

Grattan,S.R.,Maas,M.A. and Ogata,G. 1981. Foliar uptake and injury from saline aerosol. J. Environmental Quality 10(3): 406-409.

Hofstra,G. And Hall,R. 1971. Injury on roadside trees: leaf injury on pine and cedar in relation to foliar levels of sodium and chloride. Canadian Journal of Botany 49:613-622.

McCune,D.C,Silberman, D.H.Mandl,R.H.,Weinstein,L.H.,Frudenthal,P.C. and Giardina,P.A. 1977. Studies on the effects of saline aerosols of cooling tower origin on plants. J. Air Pollution Control Association 27(4):319-324.

Piatt,J.R. and Krause,P.D. 1974. Road and site characteristics that influence road salt distribution and damage to roadside aspen trees. Water,Air and Soil Pollution 3:301-304.

Talbot,J.J. 1979. A review of the potential biological impacts of cooling tower salt drift. Atmospheric Environment 13: 395-405.

Viskari,E-L. And Karenlampi,L. 2000. Roadside Scots pine as an indicator of deicing salt use - a comparative study from two consecutive winters. Water, Air and Soil Pollution 122:405-419.

4. Page 4-7,lines 14-18. Similar thoughts expressed. Suggest that the two sentences be combined.
5. Page 4-10,lines 2-3. What is 'tail water'?
6. Page 4-14, line 12. Should read "concluded that her studies----"
7. Page 4-15, lines 27-28. It is not the 'particles' that may be taken up through the leaf surface but rather some or all of the chemical constituents of the particle.
8. Page 4-17, line 27. Should read 'saprophytes' not 'parasites'.
9. Page 4-18, line 22. Should read 'benzaldehyde'
10.----------, lines 27 and 28. Define 'POPs' and 'SOCs'. While it is true they are defined later in the text, this is the first time they are mentioned.
11.Page 4-19,line 4. Should read "controls the vapor-particle partitioning)–"
12. Page 4-19, lines 14-17. A better reference than Smith 1990d is as follows:
    Geron,C.,Rasmussen,R.,Arnts,R.R. and Guenther,A. 2000. A review and synthesis of monoterpene speciation from forests in the United States. Atmospheric Environment 34:1761-1781.
13. Page 4-24,line 23. Suggest that this read "stressed ecosystems do not recover readily,and may be further —"
14. Page 4-26, line 3. Should this read "–particulate matter" rather "–particulate dust"?
15. Page 4-32, line 5. Suggest this read "Persistent organic pollutants (POPs) which are chlorinated such as PCBs,PCDFs,and PCDDs,can be"
16. Pages 4-39 to 4-41. The following is an additional reference re SUVB and crop plants:
    Krupa,S.V.,Kickert,R.N. and Jager,H-J. 1998. Elevated Ultraviolet (UV)-B Radiation and Agriculture.Springer-Verlag,Berlin,Germany. 296pp.
17. Page 4-39, lines 19-21. This needs to be rewritten. The sentence suggests that "CFC production is at a peak level now". CFC production was halted as a result of the signing of the Montreal Protocol. Perhaps what the author meant to say was that CFC levels in the stratosphere have reach peak levels and are beginning to fall as a result of the signing of the Montreal Protocol. Refer to text on Pages 4-132 and 4-133.
18. Page 4-41, line 28. What is meant by "--informed–"?
19. Page 4-46, line 22. Should read "– in field–" not –"infield–".
20. Page 4-49, line 10. Should read " – nitrogen saturated–" not "–nitration saturated–".
21. Page 4-50, lines 16-18. Unclear as worded. Something is missing.
22. Page 4-51, line 1. Has "Paerl et al., in press" been published yet?
23. Page 4-52, line 11. Should read "--Johnson and Mitchell (1998)–" not (1988). Also change in reference Page 4-174,line 14.
24. ----------, lines 20-22. Needs to be rephrased. The following is suggested. "This vegetation had been exposed to chronic low concentrations of sulfur dioxide (SO_2) and hydrogen sulfide (H_2S) for more than twenty years and then was additionally exposed to fugitive elemental sulfur aerosol."
25. Page 4-79, line 14. Should read " –(e.g., Astragalus is an —".
26. Page 4-81, line 31. Should read "—"bottom line" that is driven by an".
27. Page 4-84, Section 4.2.3. Ecosystem Goods and Services and Their Economic Valuation, lines 12-25.
    Some mention should be made of 'organics' and food chains. It is mentioned in the Summary on Page 4-158, lines 8-11.
28. Pages 4-85 to 4-86,Section 4.3.2.1 Anthropogenic Pollutants. The 'arctic haze' issue is not mentioned. The following reference is suggested:
    Barrie,L. 1986. Arctic air chemistry:an overview. In: Arctic Air Pollution, B. Stonehouse (Editor),Cambridge University Press,Cambridge,Great Britain. pp.5-23.
29. Page 4-100, lines 22-23. It is noted that there are presently over 70 sites employing the IMPROVE program monitoring methods and that it is anticipated that an additional 80 sites will be added in 2000. Since it is now 2001, how many sites are there currently employing the IMPROVE program monitoring methodology
30. Page 4-115, line 3. Should read "Metals undergo natural----"
31. Page 4-136, line 17. Should read "----and stratospheric ozone depletion."

32. Page 4-147, lines 10 -14. I believe that "the range of Rocky Mountain spotted tick vectors" already extends into the northern US states and southern Canada in the west.
33. Page 4-148, line 27. Should read "–with A. aegypti or –".

Paul J. Lioy, PhD

Chapter 3
Most of the information and analyses presented in Chapter 3 are typical of those presented in previous criteria documents on Particulate Matter (PM). Further, the analyses completed for the $PM_{2.5}$ concentrations collected with the new standard reference method are valuable as an initial assessment of annual or daily exceedences.

My major concerns are with the emissions and source apportionment sections. The focus of the emissions section is on sources of primary particulate matter. This is a good start, but is deficient with respect to sources of secondary particulate matter. The source apportionment assessment also provides more information on the nature of primary particle sources. At the same time the source apportionment analyses also point out the significant contributions of secondary particulate matter to the mass of $PM_{2.5}$, known as accumulate mode particles.

The source apportionment analyses can do an effective job investigating the percentage of contributions of secondary particles to the mass. They do not, however, provide quantitative information on the levels and types of precursor emissions which contribute to the formation of the mass.

In addition, there is no discussion on the chemistry that leads to the formation of secondary particles, and the residence time for fresh or aged secondary particles in the atmosphere. The only statement made that comes close to discussing secondary particles is on chapter 3, page 51. However, it states on line 26, that gaseous emissions "cannot be translated directly into production rates for PM." Based upon the many years of particle formation modeling that has been completed by many laboratories, this statement is not accurate.

The lack of information or predictions for secondary particle formation is serious. This is based on the information presented in the current criteria document, and many papers published since 1976, which indicate that a large quantity of the mass of $PM_{2.5}$ in many urban suburban areas includes secondary particles.

The above deficiency requires that a section be added to the chapter that specifically addresses particle formation by photochemical smog or wintertime reducing smog processes. Modeling activities that include assessments of emissions inventories and a number of chemical processes, e.g., developed by Caltech, EOHSI, and other investigators, need to be described in the section. They are necessary to establish the types and levels of precursors that lead to the formation of secondary aerosol. The section could also provide a context for coupling the efforts for controlling ozone and other pollutants, to reducing formation and accumulation of particles.

Thus, I recommend that a section be added that focuses specifically on particle formation in photochemical smog by dark phase and sunlight phase processes. It should be developed to provide the proper context for evaluating the peak concentrations observed in the summertime. Condensation and heterogeneous chemical processes and aerosol production will assist in understanding wintertime chemistry. The section should also have a discussion on products, lifetimes, concentrations, and neutralization.

The new section will provide a framework for discussion about the significance of both "soot " and "secondary particles" in causing PM air pollution. It is essential that during the development of the SIP, we do not focus on sources that will provide marginal gains in particle

control when it may be possible to benefit from ozone control strategies required to achieve the new 8-hour standard.

Some References:

Georgopoulos, P.G., Purushothaman, V., and Chiou, R. Comparative evaluation of methods for estimating potential human exposure to ozone: Photochemical modeling and ambient monitoring. J. Exp. Analy and Enviro. Epid., 7, 191-215, 1997.

Georgopoulos, P.G., Arunachalam, S., and Wang, S. Alternative metrics for assessing the relative effectiveness of NO_x and VOC emission reductions in controlling ground-level ozone. J. of the Air & Waste Management Assn., 47, 838-850, 1997.

Georgopoulos, P.G., Walia, A., Roy, A., and Lioy, P.J. Integrated exposure and dose modeling and analysis system. 1. Formulation and testing of microenvironmental and pharmacokinetic components. Env. Science & Tech., 31, 17-27, 1997.

Georgopoulos, P.G. and Seinfeld, J.H. Nonlocal description of turbulent dispersion. Chem Eng. Sci., 44, 1995-2016, 1989.

Kerminen, V.M. and Wexler, A.S. The occurrence of sulfuric acid-water nucleation in plumes: urban environment. Tellus, 48B, 65-82, 1996.

Korhonen, P., Kulmala, M., Laaksonen, A., Viisanen, Y., McGraw, R. and Seinfeld, J.H. Ternary nuclation of H_2SO_4, NH_3, H_2O in the atmosphere. J. Geoph. Res., 104, 26349-26353, 1999.

Lazaridis, M., Isukapalli, S., Georgopoulos, P.G. Modelling of aerosol processes in plumes. Tellus, 53B, 83-93, 2001.

Lazaridis, M. Gas–particle partitioning of organic compounds in the atmosphere. J.Geoph. Res., 30, 1165-1170, 1999.

Lazaridis, M. and Skouloudis A. Computer simulation of the transport, formation and dynamics of atmospheric particles. Water Air and Soil Pollution, 112, 171-185, 1999.

Lazaridis, M. and Koutrakis, P. Simulation of formation and growth of atmospheric sulfate particles. J. of Aerosol Sci., 28, 107-119, 1997.

Lurmann, F.W., Wexler, A.S., Pandis, S.N., Musarra, S., Kumar, N. and Seinfeld, J.H. Modeling urban and regional aerosols – II. Application to California's south Coast air basin. Atmos. Environ., 31, 2695-2715, 1997.

Pandis, S.N., Harley, R.A., Cass, G.R. and Seinfeld, J.H. Secondary organic aerosol formation and transport. Atmos. Environ., 26, 2269-2282, 1992.

Pilinis C. and Seinfeld, J.H. Continued development of a general equilibrium model for inorganic multicomponent atmospheric aerosols. Atmos. Environ., 21, 2453-2466, 1987.

Rao, S.T. and Sistla, G. Efficacy of nitrogen oxides and hydrocarbons emissions controls in ozone attainment strategies as predicted by the Urban Airshed Model. Water, Air, and Soil Pollution, 67, 95-116, 1993.

Roselle, S.J. and Schere, K.L. Modeled response of photochemical oxidants to systematic reductions in anthropogenic NO_x and VOC emissions. J. of Geo. Res., 100, 22929-22941, 1995.

Wexler, A.S., Lurmann, F.W. and Seinfeld, J.H. Modeling urban and regional aerosols: I. Model development. Atmos. Environ., 28, 531-546, 1994.

Chapter 5 - General:

1. The chapter on exposures is a vast improvement over the previous version.

2. The chapter provides a reasonable summary of all recent studies on exposure, and interpretative analyses of previous work.

3. Unfortunately in the attempt to be current, the authors have forgotten to put some major concepts and results into a historical context. Some of the recent studies look as if they are presenting the first set of results on a particular issue. They clearly build upon previous research. This should be acknowledged by referring to previous criteria document (AQCD, 1996) for further information on specific concepts.

4. There is still an over-emphasis on correlations. I have stated before, an "association (correlation) makes the poison" is not a valid concept. Every particle that deposits in the lung becomes part of a dose delivered to the individual. *Although the variability is very relevant to results obtained in many epidemiological studies that support PM health effects*, no one has yet shown that a constant or "quasi-constant" baseline level of PM from indoor or personal sources is irrelevant in causing health effects. This point is mentioned in the integration chapter (9), but not in chapter 5. The variable portion may provide the final stress to individuals who has had sustained contact and deposition of particles from all sources. So, both E_{ag} and E_{ig} may have partial influence on the ultimate dose affecting an individual at risk for one or more disease endpoints, especially potential acute effects.

5. The chapter needs another E descriptor, $E_{ov\text{-}rxn\text{-}iv}$ or $E_{(ioRn)}$. This is PM exposure derived from outdoor vapor (ov) reacting (rxn) with indoor vapors (iv). This is a source that could also vary with outdoor PM when the (ov) is ozone.

6. The range and distribution of many variables that affect PM penetration and deposition are nicely presented in the discussion. However, these are never integrated and placed into a final context for the uncertainties about the conclusions. The entire discussion is still attempting to steer us to a mean value for exposure used in epidemiological studies, a point that is well established. Unfortunately, the current approach ignores the distributional aspects of exposure to outdoor and other sources. It precludes further efforts in the staff paper to mention the uncertainties about the dose of specific agents or the entire mixture of PM from indoor and outdoor air, which could be relevant to acute or chronic outcomes. It precludes any discussion in the staff paper on the variety of exposures and sources, which may cause health effects. I do not believe the major ion contributing to the mean PM (e.g., SO_4^{-2}) is necessarily the chemical of concern. It may be an indicator, but we still need to define what it is an indicator of -- ambient $PM_{2.5}$ mass or toxic sub-fractions.

7. Last conclusion is a working hypothesis, but it is not the sole reason for understanding exposure. We need to eventually determine which dose or doses contribute to acute or chronic effects. The statement needs to be modified accordingly.

Detailed Comments:

P. 5.6, Table 5.1	Very good summary.
P. 5.7, Line 6	We have no definitive "outer limit" it is still a guess, and/or convenient location on the person. It is usually found somewhere within the personal envelop for inhalation.
P. 5.8, Line 21	Integral referenced to, NRC 1991. It was published previously by Lioy,

1990. Reference Lioy, P.J. "The Analysis of Total Human Exposure for Exposure Assessment: Multi-Discipline Science for Examining Human Contact with Contaminants" Environmental Science & Technology, 24, 938-945, 1990.

P. 5.11 Good summary of published activity pattern data.

P. 5.13 to 5.14, 5.3.2.2.2 Very simple explanation of mass balance model. Authors need to remind readers that all variables have ranges, and in some cases may change in value by a factor of 5 to 10. Therefore, sensitivity and uncertainty analysis are necessary when attempting to explain results.

5.3.2.3 The equation is a linear simplification of exposure and ignores possible synergisms. The authors need to provide qualifiers here!

5.3.2.3.1 Need to state that equilibrium is a simplification of indoor systems that are occupied by residents. Thus, equilibrium may only represent a "virtual" set of individuals or populations at potential risk. The alpha in Equation 5-9 can, and will, vary based upon lifestyle, meteorology, etc.

Also, need qualifiers because of personal activities, housing characteristics, and particle size and composition.

P. 5.19 Very good introduction, and Table 5.4 is well done. There are others, but most are still work in progress (e.g., RIOPA study by Weisel et al; COPD by Koutrakis, et al.). Table 5.5 good summary table.

P. 5.30 Mage – Qualify to "average person" in PTEAM.

P. 5.31 to 5.35 The net result is that there are many different types of correlations and you can get many different results. Conclusion, we still need and more work on which variable(s) is (are) needed to represent personal ambient exposure. This is essential for assessing which compounds and which exposures cause the observed effects.

P. 5.37, Lines 9-10 A low correlation doesn't mean much, $r^2 < 0.05$!

P. 5.39, Lines 29-30 Is "tracked" the right term? This only explains 25% of variability.

P. 5.41 Subjects in Baltimore were very sedentary!! Could these individuals be described as stationary personal monitors?

P. 5.41 Sulfate is an indicator of ammonium sulfate, and not even the dominant acid species (sulfuric acid, ammonia bisulfate). In areas where there are large organic, or nitrate loadings, the SO_4^{-2} ion may not be an indicator of those portions of the mass. I think SO_4^{-2} is an indicator of the variability of aged secondary aerosol in the fine fraction.

P. 5.41, Lines 26-27 Confusing. SO_4^{-2} is a strong indicator of neutralized sulfur particulate exposure, where there are no indoor sources. In contrast, $PM_{2.5}$ has many sources besides SO_4^{-2}.

P. 5.43, Lines 6-8 Is this the appropriate way to interpret these data?

P. 5.43, Lines 21-29 Please eliminate, the section does not add anything to discussion.

P. 5.45 There is an assumption that there is no cross linkage between accumulation due to chemistry outdoors, and chemistry indoors. Ozone is present indoors and outdoors. Thus part of the PM assumed to penetrate indoor could be a mischaracterization of new particle accumulation indoors, due to reactions between ozone and VOC. The reason: ozone usually varies with $PM_{2.5}$, in the summertime.

P. 5.45, Lines 21-30 Agree with statement.

P. 5-47, Lines 1-10 However, the baseline PM from primary indoor PM sources may still account for the mass burden to the lung that is built upon by the variable portion caused by the outdoor concentration and exposure.

P. 5-48 These analyses are consistent with other previous studies. Need a reference to previous document, AQCD (1996).

P. 5-49, Line 10 Need to add the BaP data in THEES. Outdoor BaP was the same at all outdoor sites across 3 sampling periods. (See attached article by Waldman et al.). Is a good study of BaP indoor/outdoor/personal exposure. It indicates seasonal differences due to sources and activities.

P. 5-51 to 5-56 These are very good sections. However, the results are discounted or ignored when the authors try to construct mean linear relationships between E_{og}, and E_{ig}, etc.

P. 5-59 Indoor air chemistry is discounted and/or ignored. If we were to put it into an appropriate context for exposure there would be an $E_{ov\text{-}rxn\text{-}iv}$ or $E_{(ioRn)}$ exposure variable for particles generated by gases outdoors, reacting with gases indoors to produce fresh particles.

P. 5-61 Good section.

P. 5-61 to 5-63 Ignored in mass balance representations. The chapter authors lean toward averaging everything to point estimates. I would recommend sensitivity analyses to begin understanding and presenting a distribution of exposure.

P. 5-67 Lines 18-19 need to be at beginning of the paragraph.

P. 5-73 Need to add the BaP exposure results from THEES (see attached article, pg. 211-215). A very comprehensive analysis, which shows a lot about seasonal variability of indoor/outdoor sources and resultant changes in personal exposure to BaP.

P. 5-78 Oglesby et al 2000, lines 11-14 is a very good analysis, and is an honest "qualitative" discussion about the uncertainties. But still ignores the fact that "association does not make the poison."

P. 5-79 (5.5.4) Ignores freshly generated aerosol indoors.

P. 5-80 (5.5.5) Good except for the lack of $E_{ov\text{-}rxn\text{-}iv}$ or $_{E(ioRn)}$.

P. 5-81 (5.6.1), Lines 8-15 Should bring to beginning of the chapter. All of page 81 is excellent, and should be moved closer to the front of the

document.

P. 5-82, Lines 15-30 Need more research and not just hypotheses to explain "paradox". In the end, there may be complex synergisms, which preclude simple decoupling of indoor and outdoor particles. Again, this does not discount the strong epidemiological "association" established and summarized in volume 2. The comment tries to direct attention to the ultimate goal of the dose to the lung and other systems.

P. 5-82, Line 28 Add – Co-generation of fresh fine and ultra fine PM from outdoor air and indoor gaseous air pollutants.

P. 5-84, Lines 6-19 The E_{nonag} may not provide the variability, but will add to the daily baseline dose received by the lung.

P. 5-84, Lines 20-27 Good point, needs to be highlighted in conclusions.

P. 5-85 Need to include $E_{ov\text{-}rxn\text{-}iv}$.

P. 5-89 to 5-92 Good analysis of the problem. The uncertainties around the various mean values or at least the variability of each variable must be part of any presentation in the staff paper.

P. 5-90, Line 30, to 5-91, Line 1-3 Still does not discount the need to consider the presence and addition of the quasi-constant non-ambient mass. Exposures will yield a dose from indoor, outdoor, and personal PM.

P. 5-91, Lines 11-14 Good point, but lines 15-19 are just as important.

P. 5-93, Lines 21-25 Very important. Should be part of conclusions.

P. 5-95, Lines 5-7 It is a working hypothesis. Needs to be stated as such here and on page 101.

P. 5-95, Lines 29-31 Point about describing a single individual needs to be made earlier. The assumption in the text is that it represents the mean, and this has to be couched by a statement on distribution functions for all variables and the need to establish a probabilistic distribution of exposure, including 95%tile.

Missing – How will exposure data be used to address causality issues. A dose from indoor/outdoor/personal exposures to fine and coarse particles will be delivered to the lung. Do we need research that looks at the incremental toxicity of each for specific endpoints, or the synergisms that can occur among various toxic compounds of each fraction?

Mort Lippmann, PhD

CHAPTER 7

Page	Line(s)	Comments
7-1	12	after "aerodynamic" replace "a" with a "comma", and after "thermodynamic", insert ", and/or electrostatic".

7-1	15-22	change "translocated" to "clearance" and vice-versa. The usage of these terms is in error, and is inconsistent with usage later in the chapter.
7-3	1	insert "components of" before "aerosols".
7-3	14	delete "a", and insert an "s" after "parameter".
7-3	16	insert "from specific sources" after "aerosols". The ambient aerosol is generally composed of multiple log-normal distributions of aerosols from specific sources.
7-3	18	change "σg" to "σg".
7-3	19	change "(or 16th % particle size to the 50th % size" to "% particle size to the 50th % size, or the 50th % to the 16th % size"".
7-3	20	delete "aerosol", and insert "of a specific aerosol" after "sizes".
7-4	21	delete "cellular", and insert "cells of airway surfaces in the" before "ET".
7-5	11	change "1 :m" to "2 :m".
7-5	13	change ">0.5 :m" to ">1 :m".
7-5	19	change "lower" to "smaller" and delete "largest".
7-5	20	change ", which" to "that".
7-5	28	change "0.3 to 0.5" to "0.2 to 1.0".
7-6	4	insert ", but their length is the factor that determines interception deposition" after "length".
7-6	6	delete "when it is electrically neutral". This is an entirely redundant statement.
7-6	9	insert "generally" before "lose".
7-6	10	delete "slowly"
7-6	14	insert "positive and negative" before "charges".
7-6	15	change "some particles may result in an" to "particles will result in".
7-6	20	change "probably" to "often".
7-7	23	insert "ET" before "deposition".
7-7	30	change "0.3 to 0.5" to "0.2 to 1.0".

7-12	8	insert "that are either very large or very small" after "particles".
7-12	19-26	The data that are cited here should be described in greater detail and/or presented here in terms of a graph or table.
7-13	8	Reference should be made here to the work of Brody et al. (ARRD 123:670-699, 1981); Brody and Roe (ARRD 128:724-729, 1983); and Warheit et al. (Exp. Lung Res. 16:83-99, 1990) indicating that particles also deposit preferentially at bifurcations of alveolar ducts in small animals.
7-13	23	insert "distal to the larynx" after "volume".
7-14	16	insert "average" before "surface".
7-14	19	insert ", and furthermore do not take the concentration of deposition on carinal ridges into account" after "effects".
7-14	28	insert "The thoracic fraction of the" before "coarse".
7-15	3,5,6,14	change "NP" to "ET" for consistency with previous text in this chapter.
7-15	14	change "lungs" to "respiratory tract".
7-16	20	change "differ in" to "have different", and insert "distributions" after "parameter".
7-17	25	insert "large airway" after "increased".
7-28	9	change "deposition" to "retention".
7-28	12	insert "at the respiratory acini" after "tissue". The importance of the existence of respiratory bronchioles in humans, but not in rodents, should be discussed at this point.
7-28	30	insert "for specific surface regions" before "that".
7-34	4-5	The sentence is incomplete.
7-37	2	insert "toxicant" before "exposure".
7-44	21	This discussion is incomplete without a further elaboration of the fact that inhalation exposure results in concentrations of deposited particles on the bifurcations of both large and small airways.
7-52	31	This discussion is incomplete without a further reference to Nikola et al. (2000), which compared retention sites in lab animals (surficial) to humans (interstitial).

7-52	31	This chapter is incomplete without a summation indicating the most critical dosimetric unknowns and those amenable to resolution by further research.

CHAPTER 8

Page	Line(s)	Comments
8-3	13-14	The cited references refer to silica. Where can the reader go for an update on asbestos? The most recent ATSDR Toxicological Profile, or Lippmann (Environ. Toxicants, 2nd Edition, 2000) could be cited.
8-4	7,8	This sentence is redundant, and should be deleted.
8-6	4,5	This sentence is a real reach. The least that is needed here is a citation to the chapter section that attempts to justify this conclusion.
8-6	11-14	A reference citation should be provided to indicate where these data come from.
8-6	27	This discussion should be a separate paragraph.
8-6	31	Change "deposition" to "retention".
8-9	2	insert "is" before "present".
8-10	8	insert "some of" after "investigating", and "may" before "cause".
8-10	22-24	This sentence is far too definite a statement!
8-19	4-10	There should be a citation here to the later discussion of the "overload" issue in this chapter.
8-21	23	This discussion beginning here and extending to p. 8-23, line 11 provides strong evidence that transition metals may not be as important as repeatedly stated elsewhere in this chapter, and should signal a more general reassessment of many of the statements made elsewhere in this chapter.
8-25	19	insert ", but growing," before "number".
8-29	5	change "human" to "humans with".
8-29	26	change "health" to "healthy".
8-30	28	The statement ".... and that PM metal content was a better indicator than PM mass" is clearly not supported by the preceding discussion! There must have been more transition metal content in the ROFA than in the Ottawa ambient PM.
8-32	13,14	The preceding discussion of Godleski's research was restricted to concentrated ambient PM, not to ROFA.

8-62	10,11	The preceding discussion does not provide an adequate basis for such a firm conclusion.
8-62	13	change "subject" to "subjects".
8-62	17	change "side" to "sides".
8-65	29,30	How does the preceding discussion provide a basis for this conclusion? It could be made in any case without citing the preceding discussion.
8-67	5	If, in fact, the 94 mg/m3 was not an erroneous value, it is difficult to understand why such an outrageous and irrelevant exposure was worth citing in the CD.
8-70	23	change "time" to "times".
8-70	29	change "scrutinization" to "scrutiny".
8-72	29	change "to" to "that was".
8-73	7	insert "some of" before "the pulmonary".
8-73	8-10	If a contrast is to be drawn, then the concentrations at issue should be cited. If the work of Amdur and colleagues were included, the conclusion drawn would be quite different.
8-73	20-22	What does the 10,000 : g/m3 refer to? It clearly was not to acid. Was it to carbon?
8-75	1	What relevance can an exposure at 15,000 : g/m3 have to the discussion? Inclusion of citations to such ridiculous exposures do not belong in this CD.
8-75	10-13	What exactly are the authors saying here? Is there a serious intent here? If so, it should be justified and elaborated.
8-85	14	What implications? We, the readers, are at least entitled to some elaboration on what the implications in the authors' minds may be.
8-86	1	delete "However," insert "low concentrations of sulfuric acid on" before "ultrafine", and insert "metal oxide" before "particles".
8-86	2	change "focussed largely on" to "demonstrated"; change ". and" to "However,".
8-86	3	insert "also" before "have".
8-86	25	Add the following: "However, ambient diesel particle concentrations have decreased during the time of increasing asthma prevalence."
8-87	12	change "has" to "can have".

8-87	20	delete "however,".
8-88		Section 8.7 SUMMARY ignored the discussion in Section 8.5.3 on "Potential Cellular and Molecular Mechanisms" (pp. 8-58 through 8-68). Was it because it had no apparent relevance to the issues at hand?... or because the results cited were too various and confusing to show how further research on biological mechanisms can be structured to advance the understandings needed to guide the identification of the physical and chemical properties of ambient PM that lead to adverse health effects. This summary section is incomplete without a reasoned summary of what previous research on biological mechanisms of PM health effects has determined, and how strategic planning for further research efforts can best be structured to resolve the unknowns in this important area.

CHAPTER 9 - INTERACTIVE SYNTHESIS - General Comment

In general, this chapter is well organized and provides a clear summary statement and synthesis of the PM literature described in the preceding chapters. It will, of course, need some fine tuning, updating, and more definitive conclusions following receipt of CASAC and public comments. It is well on its way to serving its intended purpose and represents a welcome evolution from earlier PM criteria documents.

Specific Comments

Page(s)	Line(s)	Comments
9-3	3	insert "for regulatory purposes" after "pollutants".
9-4	4	change "enter" to "penetrate".
9-4	5	change "excluded" to "retained".
9-4	11	insert "or trimodal" after "bimodal" and "minimum between 1.0 and 3.0 ：m" to "minima at about 0.06 and 2.0 ：m". The figure referred to (Figure 9-1) is clearly trimodal, even though it represents the special case of near major roadways.
9-4	13	change "the" to "that".
9-7	10	insert "and PM10 includes only those coarse mode particles that can penetrate into the human thorax" after "equivalent".
9-7	28	insert ", which are predominantly in the fine mode" after "compounds", and insert ", which is predominantly in the coarse mode" after "material".
9-9	15	insert "relatively" after "only".
9-26	1	The authors should know better than to give credence to the notion of "some exposure analysts feel that ambient concentrations represent a surrogate for total personal exposure". This is a place where what we know should take precedence over ill-considered conjecture!

9-27	17	insert "source and/or" after "each".
9-27	27	change "several" to "many (~16)".
9-28	15	change "lower" to "smaller".
9-28	22	insert "directly proportional to the number of charges" before "inversely".
9-28	23	change "likely" to "generally".
9-30	5	change "and through segmental bronchi" to ", bronchi and bronchioles". There are "hot spots" on deposition on bifurcations at all branching levels, as I noted in my review of the Dosimetry chapter.
9-30	8-10	This statement is flat-out wrong, and needs to be reconsidered. Deposition peaks in the segmental bronchi.
9-32	29	"mucociliary" is misspelled.
9-33	24	change "(< 24 h)" to "(< 10 days)". The clearance via alveolar macrophages is minimal during the first 24 hours.
9-33	26	insert "moderately" before "soluble". Highly soluble materials do not retain their particulate form long enough to be translocated.
9-35	11	change "particles" to "deposits".
9-39	15	for consistency, insert "(SOx)" after "sulfur oxides", "(NOx)" after "nitrogen oxides", and "(O3)" after "ozone".
9-66	26	The "McConnell et al" reference is to one of the papers from the CARB sponsored children's health study at USC. The reference here should be to a paper by McDonnell et al on the AHSMOG data.
9-69		Figure 9-9 There is no translation given for the "HF" and "1 HD" caption designations in the figure. They refer to congestive heart failure and ischemic heart disease respectively. This also applies to Figure 6-6.
9-74		Figure 9-10 The hospital admissions data for Detroit reported by Lippmann et al. (2000) should be included in this summary presentation data. This also applies to Figure 6-7.
9-79 and Section 9.6.2.3.3		This section is incomplete without discussion of a recent series of important papers from the Children's Health Study in Southern California. In particular, discussion needs to be added for the following:
9-80		A. Papers that were cited in Chapter 6: 1) McConnell et al., EHP, 1999; 2) Peters, J.M. et al., Am. J. Resp. Crit. Care Med., 1999b and c; 3) Gauderman et al., Am. J. Resp. Crit. Care

		Med., 2000. B. Papers not previously cited: 1. Gilliland, F.D. et al. (2001). The effects of ambient air pollution on school absenteeism due to respiratory illnesses. Epidemiol. 12:45-54. 2. Avol, E.L. et al. (submitted). Respiratory effects of relocating to areas of differing air pollution levels. 3. McConnell et al. (in preparation). Childhood asthma exacerbation and fine particulate air pollution in Southern California. Contact Dr. John M. Peters at USC for copies of these papers.
p. 9-90	11-17	The section on the ROFA studies needs to acknowledge that the effects observed were attributed to much higher concentrations than those that occur in ambient air.
p. 9-104	1-4	This discussion needs to distinguish between infants and children. Premature mortality occurs among infants (< 1 year of age) but not in children over one year of age. Excess morbidity and functional decrements are seen in children, especially those active out-of-doors. Lumping the two groups together is misleading and incorrect.

CHAPTER 6 EPIDEMIOLOGY - General Comment

The authors of Chapter 6 are to be commended for an outstanding scholarly summary and synthesis of an enormous and highly complex literature on PM epidemiology. It comprehensively reviews the peer reviewed literature and systematically addresses what is known, what is uncertain, and what issues need to be resolved by further research.

One background topic not specifically addressed is the role that past regulatory decisions on the selection of PM indices have played in the evolution of the PM epidemiologic literature base. The adoption of PM10 in 1987, and of PM2.5 in 1997, have generated ambient air concentration databases that made it possible for epidemiologic researchers to address and resolve many of the previously unresolved linkages between airborne PM and human health, and the newly authorized network of speciation samples holds promise for further advances in the near future on the identification of the more influential components of the ambient pollution mixture.

While there must, of necessity, be an end to the inclusion of newly accepted peer reviewed literature, the authors should make every attempt possible to include more of the emerging research findings as possible. In this regard, I call the attention of the authors to some of the potentially most important papers of which this reviewer is aware. In this regard, the text of this section should be expanded to reflect some recent relevant research reports, such as:

1. The report by Laden et al. on the follow-up study of the 6-cities cohort (Abstract ISEE-437, in: Epidemiol. 12(4): S81, July 2001), and the one by Pope et al. on the follow-up study of the ACS cohort (Abstract ISEE-205 in the same issue of Epidemiol.). The paper by Pope et al. (ISEE-205) describes a follow-up analysis of the American Cancer Society cohort in 51 U.S. cities for 16 years of mortality experience will report significant associations between PM2.5 and both cardiopulmonary and lung cancer mortality. (The Abstract that appears in Epidemiol., July 2001 does not describe the recently completed analyses.) There were no associations of mortality with the coarse thoracic mass (PM10-2.5).

2. The paper by Künzli et al. on the justification for relying on the cohort mortality studies for the best estimates of PM-related premature mortality (Am. J. Epidemiol. 153(11): 1050-1055, 2001).

3. Research reporting significant PM-related infant mortality to supplement the previous paper by Woodruff et al. (1997). These include an 8-city study (in the U.S.) by Kaiser, Künzli, and Schwartz (Am. J. Respir. Crit. Care Med. 163(5): 881, Apr. 2001) as well as 2001 ISEE Abstracts (Epidemiol. 12(4), July 2001). One, by Ha et al. (ISEE-134) describes PM10-related mortality in Seoul, Korea. Two others describe PM10-related reductions in birthweight, which provide coherence support for premature mortality. Bobak (ISEE-209) provides data for the Czech Republic, and Wojtyniak et al. (ISEE-331) provide data for Poland.

4. Research on the effect of PM on the health of children in Southern California beyond those reported in the PM CD draft. These include:

a. Gilliland, F.D. et al. (2001). The effects of ambient pollution on school absenteeism due to respiratory illnesses. Epidemiol. 12:45-54.

b. Avol, E.L. et al. (submitted). Respiratory effects of relocating to areas of differing air pollution levels.

c. McConnell et al. (in preparation). Childhood asthma exacerbation and fine particulate air pollution in Southern California.

Contact Dr. John M. Peters at USC for copies of these papers.

Specific Comments on Text

page	line(s)	Comments
6-4	12	add to end "while NO2 contributes to the formation of organic aerosols during photochemical transformations.
6-6	11	The generally accepted abbreviation for coefficient of haze is "CoH", not "COH".
6-7	7	insert "annual average" before "commmunity".
6-7	15	insert "short-term" before "mortality".
6-7	22	insert "than average" before "relative".
6-11	12	insert "Short-Term" before "Information".
6-39	1	change "most" to "nearly".
6-39	5	insert "are" before "generally", and change "comport" to "consistent".
6-80	14	insert the following sentence after "mortality". "On the other hand, the ACS cohort was largely Caucasian and above average in a socioeconomic sense, and its mortality RR would be expected to be lower than a more representative U.S. population".
6-83	1	delete "out".

6-105	7	change "newly" to "later".
6-108	26	change "constituent" to "index".
6-132	8	change "which" to "that" (also p. 6-184, line 26; 6-205, line 10).
6-138	7	change "which" to "that" (also p. 6-269, line 24).
6-140	18	change "is" to "are".
6-141	18	insert ", the variability of pollutant concentrations within the community," after "sites".
6-172	8	after "associations", insert the following words from line 9: "have been reported by several investigators".
6-172	31	insert "those" after "than".
6-175	15	transpose "U.S." and "various".
6-175	19	delete either "Both" or "jointly".
6-175	27	delete "Turning to non-U.S. studies". This study involved a mixture originating, at least in part, in the U.S., and it was based on the same kinds of measurements and models used in U.S. studies.
6-180	13	insert "hospital" after "asthma".
6-183	29	insert "in one second" after "volume" and change "FEV" to "FEV1".
6-184	10	change "PF" to "PEF".
6-184	16	change "PF" to "PEF".
6-205	20	delete "As" and "other".
6-218	3	change "that" to "which".
6-225	28	insert "to be" before "expected".
6-228	4	This section (6.4.2.3.) should not end without some interpretive statement and/or identification of what additional investigation is needed to make this alternative approach more useful for analyses of PM source impacts on human health.
6-228	25	insert "cohort" before "study".
6-229	11	insert "large" before "U.S.".
6-230	12	transpose "as the exposure metric" with "a three-day running average".

6-243	12	This section (6.4.4.) should not end without a discussion of which approaches might resolve this important issue.
6-267	2,10	insert "thoracic" before "fraction".
6-267	15	insert "well" before "beyond".
6-268	20	insert "thoracic" before "fraction".
6-268	28	change "may not yet be" to "are not yet".

Jane Q. Koenig, PhD

Chapter 6

I complement the authors on an ambitious and generally successful job of summarizing recent studies in the field of epidemiology. I do have some major concerns.

Major

1) In my opinion, this chapter includes an unacceptable amount of editorial comment. It is my understanding that the purpose of the CD is to summarize the scientific literature and that comments and critiques of that literature are reserved for the Staff paper.
2) I know of at least two important papers that were not included in the document. This is of concern as there may also be others that I didn't notice. What was the process for inclusion of studies?
3) It is disturbing that the health effects of exposure to PM from wood smoke or other vegetative combustion sources are not mentioned. Wood smoke health effects should have been included in section 6.5. I believe this is a major oversight that should be corrected.
4) Apparently there is no discussion of potential associations between PM exposure and cancer. This may be an oversight.

Other general comments

Table 6-1 contains too much text. I think it detracts from the usefulness of the table (which is to provide an easily read comparison of data). This problem is present in the other large tables in the chapter as well. Would Table 6-1 be more useful if there were columns for lag times, RR, etc that are easy to scan? A table of significant associations between gaseous pollutants and mortality would be useful. I suggest notation of effects seen at concentrations below the current PM10 and proposed PM2.5 standards throughout the chapter.

5-1 2nd sentence, I think cardiac dysfunction should be mentioned right up front

5-45 Mar et al. gases were more highly correlated with PM2.5. PM2.5 and CO corr =0.85, with NO2 corr = 0.79 than noted in the CD

5-45 bad idea to use county for the unit. Certainly in King co people in gold Bar are not exposed to what Beacon Hill measures!! This is an example of using quick and easy to obtain data sets. Maricopa county appears to give very different outcomes than Phoenix.

5-46 -recommend that composition comments here be moved to 6.2.2.4

Table 6-16 This table would be more useful if the Emergency Dept studies were separated from Hospital Admissions. Also in general the tables in the Morbidity section are much easier to use than those in the Mortality sections.

Table 6-23 Respiratory Sx, lung function and biomarker effects.. What biomarkers are investigated? I didn't find any. Table 6-22 (asthmatic subjects) is entitled just Sx and lung function.

6-216 6.4.1 This section appears to belong in ch 9??

5-225-227 Is it commonly accepted that SO2 cannot be a confounder for PM???

5-226 Discussion of the use of factor analysis is a good addition.

5-238 Mention of the Lipsett (1997) study is an opportunity to mention the role of wwod smoke as a constituent of PM. This should have been emphasized. In general there is not enough use of the role of geographical differences in PM composition as a means of understanding the toxic components.

5-246 Discussion of thresholds. If individual responses to PM prevent establishment of a threshold, how does that fit with the language of the CAA that requires setting a NAAQS for the most sensitive members of society??

5-266 6.5 Conclusions

2. Would it be more useful to describe heterogeneity as geographic differences in the composition of PM?

#3 I think short term v long term exposures need to be considered very, very carefully. We do not know to what extent prior exposure to air pollution is involved in the premature death cases in the short-term time series studies.

#4 The CF data may be telling us that there are geographic differences in PM

#5 This conclusion highlights effects during early pregnancy and post-natal periods. However these data are not presented forcefully in the prior text of the CD.

#9 As I mentioned earlier, I suggest a systematic description and summary of effects of co-pollutants.

#12 this paragraph (or a separate one) could include a discussion of the fact that there are likely different mechanisms for different PM-induced health effects. For instance, the mechanisms underlying air pollution aggravation of asthma will be entirely different from those underlying death from congestive heart failure.

#13 Should this paragraph be merged with # 4?

Comparison with the November 1999 draft CD

1) CASAC deemed that draft to be too encyclopedic and yet I don't see that the current draft is any less so.
2) CASAC recommended emphasis on cardiovascular effects and on infant mortality. I expected to see a separate table for these outcomes—certainly for infant mortality as there are only a few studies.
3) Is there really any more risk assessment in this draft than in the 1999 draft?
4) I believe that the strategy used to select the articles cited in the CD is still lacking in spite of a specific request following the last meeting of CASAC.

Chapter 5. Human Exposure to PM and its Constituents

I am not by any means an expert in the filed of exposure assessment. That said here are my impressions on this chapter.

My overall impression of this chapter is that it is very different in scope from chapter 6 and 8. The emphasis appears to be a description of models available for describing exposure. As with chapter 6, this chapter would benefit greatly from a short paragraph at the beginning describing the goals and intent of the chapter. As with Ch 6 I am disturbed that the data on wood smoke have not be considered. The indoor/outdoor studies of fine PM from wood smoke may offer some useful information on penetration of PM indoors.

Another impression is that the chapter listed individual papers published since 1996 but did not compare and contrast these studies.

Specific comments

4-1 The second sentence should state that the lung AND HEART are the targets of concern.

4-4 Is the nomenclature μe accepted in the field. I don't like it—micro environments have nothing to due with scientific measures of micrometers etc.

at) In all figures the authors need to be very clear not are measured data and what are deduced from the models.

Should there be some description of exposure assessment to co-pollutants?

Petros Koutrakis, PhD

Executive Summary:

This has not yet been provided by EPA.

Introduction:

The introduction is very informative and concise. I agree with the approach to build upon the recent 1996 Criteria Document, which made it possible to focus on recent information. Considering that the number of publications on particle exposures and effects has increased exponentially over the last few years, I was afraid that the new Criteria Document would be larger than the yellow pages. I am very pleased to see that this is not the case and the EPA staff have provided, for most of the Document, a critical review of the existing information rather than merely a catalogue of papers. It is clear that the particle health effects field has significantly matured and that the continuing interactions between EPA and the research community have helped to build a scientific consensus. This is very gratifying and will enable us to address this serious public health issue in a cost effective way.

Chapter 2: Physics, Chemistry, and Measurement of Particulate Matter

Overall, this chapter is very well written. As indicated in my previous review, I had only a few comments which now have been addressed by the authors. In addition, the authors have referenced many recent papers relevant to this chapter.

To obtain organic carbon total mass concentration it is necessary to multiple the carbon concentration (detected as OC) by 1.4. This conversion factor corresponds to an average molecular weight ratio of ambient air organic compounds to carbon. Because this conversion factor can depend on aerosol composition, which can vary by time and location, there may be

substantial uncertainty in the organic carbon measurements. I do not remember whether this issue was addressed in this chapter. If not, this is an important topic that should be discussed extensively. These inherent organic carbon measurement uncertainties may make it more difficult to reach particle mass closure.

This chapter would be better if the discussion about carbon was a little more concise. In contrast, the discussion on the elemental analysis, pages 77-80 is only rudimentary. If the authors do not want to give many details about the methods, this is fine, but at least they should discuss the advantages and shortcomings of these methods. A more critical discussion is appropriate because elemental tracers are of paramount importance to source apportionment studies. The problem (which is good news from the health effects perspective) is that trace element concentrations have decreased and XRF may not be the most adequate method, although is the most practical one. Reading this section one cannot find a take-home message about the state-of-science in this area.

Below are some minor specific comments:

Section 2.2.1.5; It may be worthwhile to report some results from the compliance network. I know OAQPS has results from the FRM audits. I think it is important to mention something about the precision of the FRM sampler under real ambient conditions as operated throughout the country by different states.

Page 2-64, lines 7-8; I am not sure if this statement is correct.

Page 2-73, line 10; Particle/particle interactions also are very important. For example, the reaction between ammonium nitrate and sulfuric acid or other acid sulfate particles can result in the formation of nitric acid vapor that can be lost from the filter. Of course, it is not thermodynamically possible that ammonium nitrate coexists with acid sulfates in the atmosphere. However, during the collection of a multi-hour sample, e.g. 24 hours, these compounds can be present in the atmosphere at different times and thus can be collected on the same collection medium

Section 2.2.5; There was in inter-comparison study of continuous methods supported by CARB in Bakersfield. Some of the findings from this study should be presented here, since this is one of the most comprehensive continuous particle methods inter-comparison studies.

Page 2-91, line 22-until the end of the sections; Too many details are presented here and I do not understand the point being made.

Page 2-94; A section on continuous sulfate measurements should be included. Discuss the old FID method and the new Fluorescence method which will be used by most of the supersites (by Allen et al, Harvard University).

Page 2-97; The discussions on data quality is very superficial and incomplete. I suggest to fix it or drop it.

Page 2-102, lines 24-26; Need to eliminate. The authors have been made a big deal of this throughout the chapter.

Page 2-105, lines 4-5; This sentence does not mean anything, therefore I suggest to eliminate it.

Chapter 3: Concentration, Sources, and Emissions of Atmospheric Particulate Matter

The revised chapter has been considerably improved. The authors considered most of our previous comments. They have used more recent information and have expanded the scope of

the chapter. Many of the poor quality figures have now been replaced. The addition of the appendices has strengthened the chapter. I really enjoyed reading them. Although they were long, I found them very informative and am sure many people will use this information.

The summary section needs some improvement. It should be more comprehensive and contain a good synthesis of the presented information. It does not read like a good summary, rather it only presents some highlights of chapter 3. The summary section should include a concluding paragraph on the background concentrations. In the main text the authors presented a nice discussion on this topic, but it was not clear what was the bottom line on this issue. Therefore, one would also expect some mention of this in the summary.

The weakest part of the chapter is the discussion about emissions and their trends. I know this is a very difficult topic and the existing information is very limited. For this reason the NRC committee on particle research has recommended that EPA investigates particle source emission in a comprehensive manner. The chapter does not acknowledge this lack of information, rather it tries to make a good story which is not there. The introduction of the emission section is confusing and the discussion on uncertainties is rudimentary. Some discussion on methods to measure emissions may be worthwhile to include. Also some discussion about the importance of biogenic sources would be worth including.

Below are some minor specific comments:

Table 3-1; Do the percent contributions correspond to sulfate and nitrate or to ammonium nitrate and ammonium sulfate?

Figure 3-1; This figure is not clear. It is hard to distinguish the solid circles. Same for Figures 3-4a and 3-4b. It is really hard to read these figures.

Figure 3-2; How were the nationwide trends calculated? Were the lines in the figure interpolated between the two successive years or are they moving averages?

Page 3-10, line 7; ..acids. Define which acids.

Page 3-10, lines 24-27; This sentence is not clear.

Page 3-12, lines 6-8; This sentence is not clear, needs editing.

Table 3-8; These studies should be sorted: alphabetically, chronologically, or geographically.

Page 3-49, section 3-4; This section is not well written. What is the message here? This section is confusing.

Figure 3-23; The title of figure should read “PM2.5 Total Primary Emissions....”. It should be clear that this table presents only primary emissions.

Page 3-53; In lines 21-24 you mentioned that sulfate concentrations decreased less than the corresponding sulfur dioxide (I agree with this statement). However, in Table 3-10 sulfate decrease is 39% and sulfur dioxide is 16%. Something is wrong here?

Table 3A-1; This is a very useful table. It would be nice (if it can be done easily) to include the OC/EC ratios for the different sites.

Page 3B-1; In the first three lines you use three times the word “discuss/discussions”.

Page 3B-24, line 19; Use = instead of - for sulfate.

Chapter 5: Human Exposure to Particulate and its Constituents Introduction

This chapter has now been substantially improved and the authors should be commended for their efforts. A comprehensive review of the most recent exposure studies has been included in this chapter. My remaining criticism for this chapter is that although it presented a very comprehensive review of personal and indoor particle studies, it failed to critically synthesize this information. What are the most important conclusions that this chapter should highlight? In my opinion the following points need to be clearly made:

a) Personal exposures are associated with both indoor as well as outdoor sources; b) the personal exposure/outdoor concentration ratios present substantial intra- and inter-personal variability; c) Although we originally thought that this variability was mainly due to the presence of personal and micro-environmental sources, the results from recent exposure studies suggest that it is the varying impact of the outdoor particles on indoor environments that is mainly responsible for the observed intra- and inter- variability in personal exposure/outdoor concentration ratios and; d) It appears that home characteristics may be the most important factor that affects the relationship between the average population exposures and ambient concentrations. Air exchange rate seems to be an important home characteristic surrogate that can explain a large fraction of the observed inter- and intra-personal variability.

These findings explain why longitudinal studies (many repeated measurements per person) provide stronger correlations between personal exposure and outdoor concentrations than cross-sectional studies (few repeated measurements per individual). Since home characteristics is the most important factor affecting personal exposures then one would expect that correlations between average population exposures and outdoor concentrations will vary by season and geography. To test this hypothesis, Janssen et al. 2001 (Environmental Health Perspectives, in press) examined the relationship between Hospital admissions (for cardiovascular and respiratory diseases) in a large number of US cities (NMMAPS study) and found that central air conditioning use explains a large fraction of the variability among cities.

Also one important issue that should be stressed in this chapter is that multi-pollutant personal exposure studies have suggested that ambient concentrations of gaseous co-pollutants are surrogates of personal exposures to particles rather than confounders (Sarnat et al. 2001, Environmental Health Perspectives, in press).

However, because the authors have provided a reasonable and objective interpretation of the findings of the existing exposure studies, it will not be difficult to fix this chapter. This can be easily done by revising the summary section and by providing some critical discussions throughout the chapter.

Throughout the chapter the authors discuss the distinction between outdoor and indoor sources. Although I agree with their approach and that this should be presented, I disagree with their decision to make this the central issue of the chapter. I think there is some exaggeration here.

Finally, the discussion on the exposure error is an important one, but I think it needs to be concise and straightforward. Many people do not have the background to understand this discussion which is very important.

Specific minor comments:

Page 5-2, lines 1 and 14-15; need editing.

Page 5-14, line 5; P and k are also function of home characteristics, not only particle size and air exchange rate. Same comment for Fint, see page 5-16, line 4.

Page 5-17, equation 5-10; the coefficient a in this equation is not constant and presents substantial intra- and inter-personal variability.

Page 5-18, line 4; This statement is wrong. The chapter contradicts itself, see Figure 5-2 on page 5-44.

Same page, line 7-9; This is not fully correct. It is not just the physical and chemical properties of particles, house characteristics are also important.

Title 5.4.1; change to: Types of Particulate Matter Personal Measurement Studies.

Page 5-19, line 24; I do not understand what is the daily average? I know you describe this on page 5-31, but I still find it confusing.

Page 5-22, line 14; "many studies..." This is not true.

Section 5.4.2.3 on page 5-24; short and not-well written interpretation of particulate matter exposure data.

Figure 5-46; If I remember well they used sulfur to calculate the fraction of particles associated with outdoor sources. But we know that the S may not be a good tracer for ultrafines and coarse particles, there fore, the results presented at this figure should be presented with caution.

Page 5-47, lines 17-19; if personal activities include closing or opening the door and windows, then these activities will impact the non-ambient levels.

Page 5-24, line 19; fix nitrate and ammonium, same thing for table 5-13.

Page 5-86, lines 1-2; There is a recent paper by Long et al. 2001 (Environmental Health Perspectives, published) that compares the toxicity of ambient and indoor-generated particles.

Page 5-98, lines 11-12; please see my previous comment on the variability of sulfate personal/outdoor concentrations.

Chapter 9: Integrative Synthesis: Particulate Matter Atmospheric Science, Air Quality, Human Exposure, Dosimetry, and Health Risks

The first 23 pages is "the best of chapters 2 and 3". It is nicely done but I do not see the synthesis.

Section 9.4, summarizes the entire human exposure chapter 4. This is relatively short compared to the presentation of chapters 2 and 3. This is fine because I think that it is the first 23 pages which need to be substantially truncated. Again the authors failed to deliver the synthesis of the exposure studies to date. Please see above my main comment for chapter 4.

The dosimetry section, 9.5, was very concise and informative.

Page 9-44, lines 30-31 and next page lines 1-2; Janssen et al found that the % of PM10 associated with vehicular emissions and the fraction of homes using central air conditioning per city explained most of the heterogeneity among NMMAPS cities (Janssen et al. 2001, Environmental Health Perspectives, in press).

The section on epidemiology is too long. Again this reads like the best of the epidemiology chapter.

The rest of the sections are fine.

Overall, I think the different chapter sections should be balanced and use the same approach. Sometimes this chapter reads like a very long summary rather than an integrative synthesis and definitely there is very little connective tissue among the different sections. In other words, one could place each of the sections at the end of the corresponding chapter as a summary. I hope the executive summary (which I have not seen yet) will provide some real synthesis and a discussion which expands across disciplines.

Roger McClellan, DVM

OVERALL COMMENTS

The present draft represents a significant step forward in summarizing the current status of knowledge on the health effects of ambient particulate matter (PM). However, the present version is not an adequate review and synthesis of the information on PM required for establishing the indicators, level, averaging time and statistical form of National Ambient Air Quality Standards for PM.

The document will be improved by using the "source to health responses" paradigm shown in the NAS/NRC PM report as an integrating structure for the Criteria Document.

In my opinion, the document tends to overstate positive associations between increased levels of ambient PM and increased rates of mortality and morbidity and does not always convey the high degree of uncertainty in the date. While the NMMAP study represents a substantial advance in our identification of PM in some locales as having hazardous properties, the high degree of variability in effects estimates across the U.S. with lack of statistical significance in many cities suggests caution in interpreting relative risks of less than 1.1 and certainly for relative risks of less than 1.05. The use of normalized values of 50 : g/m^3 for PM_{10} and 25 : g/m^3 for $PM_{2.5}$ and $PM_{10-2.5}$ tend to exaggerate the actual findings. This could be illustrated by constructing a table presenting the actual estimated relative risk in percentage relative to the 10^{th} to 90^{th} percentile (or 25^{th} to 75^{th} percentile) range of the PM measurements.

The CD needs, in multiple places, to offer an admonishment that the quantitative statement of effects estimators, while useful for comparing and interpreting data, should <u>not</u> be used to make "body count" estimates or predictions for any city or region and certainly not for the U.S.

CHAPTER 6 - EPIDEMIOLOGY – GENERAL COMMENTS

In general, this chapter provides a comprehensive survey of the epidemiological studies that have analyzed for PM associated health effects. However, the chapter can and should be improved to provide a more balanced presentation of the current information available on the human health effects of PM.

The chapter could be improved by development of an expanded introduction. Three key elements of an expanded version would be sections on (a) baseline health statistics, (b) the issue of inter-city and intra-city (temporal) variations in air quality and (c) analytical methods and statistical considerations. All three of these issues become critical to the conduct and interpretation of epidemiological studies. The baseline health statistics data are covered in a cursory manner in Chapter 9. That information should be presented at the beginning of Chapter 6 in an expanded format. To help the reader appreciate inter-city variability in health, a distribution histogram might be developed of the cardiovascular and respiratory death rates for the 88 cities in the NMMAP study. It would be preferable to show the rates for cardiovascular and respiratory deaths separately, rather than combining them as done in Table 6A. To illustrate intra-city temporal trends, the figure from Kelsall et al (1997) showing mortality data (1974-1988) for Philadelphia should be included.

For air quality data, distribution histograms could be developed for PM_{10} from the NMMAP study data to illustrate inter-city variability. The intra-city (temporal) trends could be

illustrated using a figure from Kelsall et al (1997) for multiple pollutants for Philadelphia (1974-1988). The inclusion of these figures will help to illustrate the challenge faced in "teasing out" air pollution impacts from other factors that influence mortality (and morbidity) from respiratory and cardiovascular disease.

The above discussion would lay the general groundwork for the section on analy5tical and statistical considerations. In this reviewer's opinion, the most significant advances since the 1996 CD are derived from the NMMAP study. This study benefited from the use of a common database and a common analytical methodology as well as increased statistical power related to analysis of data from 88 cities over a relatively long time period (1987 – 1994). A brief discussion of the analytical methodology used in conducting the NMMAP study and related studies would be helpful to the general reader who is not an expert in epidemiology.

The balance in the chapter could be improved by giving more attention to issues of statistical certainty/uncertainty. The authors have tended to call attention to statistically significant results while tending to avoid calling attention to the lack of statistical significance in other studies. The authors need to do everything possible to ensure that all studies are reviewed and reported in an even-handed manner. If certain studies are given "special weight," the basis for doing so should be clearly articulated.

The present draft does not adequately treat the issue of co-pollutants and conveys a view that the authors are zealous in putting PM center stage and pushing other pollutants into the background. For each study, the CD should clearly state whether the analytical methodology considered only some indicator of PM or also considered co-pollutants. For each of the various endpoints, tables should be created that would include more detailed information from the studies that considered co-pollutants. This would include presentation of the relative risks for the other pollutants when they were determined.

The present draft does not adequately treat the issue of heterogeneity of effects estimates, especially as reported in the NMMAP study. While it is correct to say that the basis for city to city differences in effects estimates is unknown, more attention should be given to elaborating on potential explanations for the differences. This would include the possibility that the differences are real and the levels of PM_{10} present in certain cities did not yield statistically significant effects estimates for PM_{10} for the period studied (1987-1994).

CHAPTER 6 - EPIDEMIOLOGY – SPECIFIC COMMENTS

Page 6-3, line 18: "Confounding and Effect Modification." This section addresses a very important point when it notes that "the health outcomes attributed to particles are not very specific." Indeed, the modifier "very" could be dropped to make the statement more accurate. It would be helpful to the reader to illustrate the extent to which the majority of the typical health outcomes are attributable to other factors. Indeed, the terms – confounders and effects modifiers – do not adequately relate the extent to which the health outcomes are attributable to factor others than the identified modifiers and effects modifiers.

Page 6-5, lines 28-30 and **page 6-6, lines 1-2**: It would be useful to add a paragraph or two here placing the pollutant increments in perspective. For example, for most of the U.S. increments of 50 : g/m^3 for PM_{10} or 25 : g/m^3 for $PM_{2.5}$ are not at all representative. The use of these increments tend to present an exaggerated view of PM effects. I suspect that is why the NMMAPS authors elected to normalize their results to 10 : gm^3 of PM_{10}.

Pages 6-6 and **6-7**: The approach used through the document of discussing the 1996 CD findings and then the post 1996 CD finding is confusing. I would prefer to see all of the evidence "weighed" to reach a current conclusion. The integrated finding could then be compared to the 1996 CD findings.

Table 6-1. The table should be expanded to include information on the effects estimators for pollutants other than PM when the individual study has evaluated other pollutants. Alternatively, this could be done in a separate table for those studies which have looked at

multiple pollutants. In presenting the results, it would also be useful to complement information on pollutant effects estimators with information on actual pollutant levels so that the role of the individual pollutants would be more apparent.

Page 6-42, line 7 and **page 6-43, line 6**. It would be useful for the CD to include an expanded discussion of the handling of county-specific variables and co-pollutants in the NMMAP studies. Specifically, it would be useful to include one or more tables that present specific data on the effects estimators used for other pollutants such as NO_2, O_3, SO_2, and CO and for temperature (both elevated and reduced). This would be helpful in understanding the total air pollution effect and the relative importance of PM. It is not sufficient (as in page 6-44, line 2-3) to relate that the PM_{10} effect on mortality "did not appear to be affected by other pollutants in the model."

In presenting the NMMAPS results it would be useful to include a graphical display that conveys the slope of the effects estimators for the 90 cities. At a minimum, the regional data could be plotted relative to the measured range of PM_{10} values used to derive the effects estimators. The latter values might be the 25^{th} to 75^{th} or 10^{th} to 90^{th} percentile of the PM_{10} values that were used in the analyses plotted on the horizontal and the mortality rate on the vertical.

Page 6-49, section 6.2.2.4 (The Role of Particulate Matter Components). This section should either begin with or end with a discussion of the challenge of characterizing the role of specific particulate matter components. Two major issues should be covered. First, epidemiological analyses can only be carried out on the components that have been measured. In that regard, a major problem relates to the past excessive domination of monitoring by concern for regulatory compliance, with a progression in the U.S. from TSP to PM_{10} and most recently to $PM_{2.5}$ measurements and with measurements of PM indicators made only every 6^{th} day. The ability to test for the role of other components that may be significant will continue to be dependent upon having long-term measurements of these components. The second issue is the challenge of teasing out very small relative risks. It is apparent, and especially from the staff paper, that large study sizes are needed to obtain relatively stable and statistically significant results—studies for which the product of number of mortality/morbidity events per day multiplied by the number of days monitored is at least 10,000.

Page 6-58, lines 19-20: The statement indicating that wind-blown endotoxins and molds are contributing to PM10-2.5 fraction effects in the Phoenix area needs to be supported by references or omitted if it is mere speculation.

Page 6-58, line 2.7. In view of the role of SO_2 in the Wichmann, et al (2000) study, it would be appropriate to give an indication of the SO_2 levels measured and how they compare to levels measured in the eastern U.S.

Page 6-67, Source-Disputed Evaluation: It would be useful to review the analyses done by the NMMAPS investigators (perhaps even unpublished analyses) to determine if any of the results provide any insights into source-oriented impacts. For example, did the NMMAPS investigators explore any weekday versus weekend effects that might give insights into mobile source related effects?

Page 6-72, line 1: Show the Confidence Interval for excess other deaths; i.e., 1.3% increase per 50 $\mu g/m^3$ PM_{10}. It would also be appropriate to expand the discussion of other deaths to consider regional differences.

Page 6-73, lines 28-30: It would be useful to expand the discussion of sample size issues for sub-categories of disease. This could be done using the study size calculations in the staff paper for the NMMAP study showing how the study size decreases progressing from total mortality to cardiac to respiratory causes because of decreases in number of events. This discussion could be

tied back to the base-line health statistics presented in Chapter 9 (tables 9-9 and 9-10).

Page 6-77, lines 23-26: The summary statement on biogenically-derived particles in the $PM_{10-2.5}$ fraction in this reviewer's opinion is over-stated relative to the evidence. If the statement is retained, it must be backed up with specific evidence.

Page 6-80, lines 5-6: In view of the emphasis given to the relative risks for $PM_{2.5}$ derived from the ACS study, it would be useful to briefly describe the methodology used in the ACS study to arrive at $PM_{2.5}$ values.

Pages 6-86 and **6-91** were missing from all copies of the CD provided to me.

Page 6-102, line 17 to **page 6-103, line 4**: It would be useful to give the low, medium, and high PM_{10} levels studied as an aid to relating the research to contemporary PM_{10} levels in the U.S.

Page 6-133, Individual-Level Studies of Cardiovascular Physiology. This section could be strengthened by including a discussion on the statistical problems of detecting small increases in "signals" for "low prevalence effects." This could be done by considering the minimum study sizes needed to give statistically significant effects for cardio-respiratory mortality (per staff paper) and then applying these minimum sizes to the individual level studies that sought to identify more subtle morbidity indicators.

Page 6-175, line 15 to page 6-176, line 17: In discussing the association of increased levels of PM and other pollutants with asthma, it would be useful to include information on the effects estimators for the other pollutants used in the various analyses. This will place the PM effects in perspective relative to other pollutants.

Page 6-177, line 27. This discussion needs to be expanded and integrated with data presented in tables 9-9 and 9-10.

Page 6-222, line 3: This would be an appropriate place to discuss the effects estimators for PM_{10}, O_3, NO_2, SO_2, and CO, provide an indication of typical levels, and discuss the relative contribution of each of the indicators to the total air pollution effect.

Page 6-245, Section 6.4.6, New Assessment of Threshold in Concentration-Response Relationships. The issues that should be discussed in this section go well beyond considering thresholds. This reviewer suggests the section be re-titled – "Ambient Concentration – Response Relationships for PM Indicators." This is not merely an issue of threshold versus linear relationships. The discussion should start with presentation of information on background levels of PM_{10} and $PM_{2.5}$, discussed elsewhere in the CD, and how one bridges from background levels to ambient concentrations that show excess risk.

The discussion could then proceed to consideration of the range of PM indicator concentrations evaluated. This might include population-weighted data for some studies, such as the NMMAP study. The section should include a summary statement concerning the calculation of population impacts of PM exposure. In my opinion, this would include a statement concerning the inclusion/exclusion of lowest quartile or lowest half of ambient levels of PM in calculating PM impacts for populations.

Page 6-258, line 29, Heterogenicity of Particulate Matter Effects Estimates: The section could be improved by providing additional baseline data, especially relative to the NMMAP 90-city study. This could include inclusion of a table showing the average baseline rate (total mortality, cardiac and respiratory) for each of the cities studied, along with total population size. The baseline mortality for each cause might be shown for each city since this was the base

against which changes associated with PM_{10} were evaluated. In presenting data on heterogenicity, it would be of interest to include data on cigarette smoking for each city and/or region, recognizing that cigarette smoking is the largest factor driving cardio-respiratory baseline rates.

Page 6-268, lines 3-6: This statement needs expanded discussion. If the effects estimates for PM_{10} hospital admissions are higher than the effects estimates (percentage-wise) for PM_{10} mortality, does that imply that PM is more effective (than other underlying risk factors) in causing hospital admissions as compared to mortality? If so, what is the potential explanation?

Page 6-269, line 3. Useful to add a sentence "However, the statistical association of health effects with PM acting alone or with other pollutants should not be taken as an indicator of a lack of effect of the other pollutants. Indeed, the effects of the other pollutants may be greater or less than the effects attributed to PM."

Page 6-269, line 19: I suggest you omit reference to the APHEA study at this point in the document. While being a useful study it should not have nearly the same influence as the NMMAP study in terms of relevance to the U.S. The quality of the aerometric data was much poorer than that used in the NMMAP study.

Page 6-270, lines 4-7: This broad statement sounds intuitively appropriate. However, I suspect it is supported by very little data and the data were not reviewed in the CD.

Page 6A-2, Table 6A-1. For completeness, also present the data as rates; i.e., CVD deaths per 10^6/day. This will help in examining heterogenicity.

Page 6A-11: It would be useful in the interest of completeness to include the table shown as Appendix A, Table 4 in the Staff Paper in the CD.

CHAPTER 7 - DOSIMETRY – GENERAL COMMENTS

This chapter is a useful summary of what is known concerning the dosimetry of inhaled particles. However, the chapter does not have as strong a linkage to the rest of the CD and to the issues of setting a NAAQS for PM as is needed. The chapter would be substantially improved by providing a better linkage to aerosols characterized with PM_{10} and $PM_{2.5}$ samplers at the beginning of the chapter. At the end of the chapter, it would be useful to have a section summarizing what can be predicted as the total deposition and regional deposition and retained burden for various exposure conditions likely encountered in the ambient environment. This should be done by using various PM indicators, i.e., PM_{10}, $PM_{10-2.5}$, and $PM_{2.5}$. In doing the analysis, it is important to recall that the indicator measurement does not describe the total PM size distribution and mass. For example, continuous exposure to ambient air characterized as having either 30 :g/m^3 of PM_{10}, 15 :g/m^3 of $PM_{10-2.5}$, and 15 :g/m^3 $PM_{2.5}$ will yield the same total deposition irrespective of which indicator was used assuming the size distribution was the same in all three cases. It will also be important for the normalized calculations to be done for a few key PM constituents.

Throughout the chapter, care should be taken to describe deposition relative to particle size as probabilistic phenomena. This will help in conveying the correct view that particles from 0.5 to more than 10 :m can penetrate to and deposit in the nares, tracheo-bronchial region, small airway, and alveoli—it is only the probability of doing so that changes.

CHAPTER 7 - DOSIMETRY – SPECIFIC COMMENTS

Page 7-2, line 28, 7.1.1 Size Characteristics of Inhaled Particles. This section needs to be expanded to provide a linkage to measurements of PM_{10} and $PM_{2.5}$. In its present form, this section is disconnected from the rest of the CD.

Page 7-4, Structure of the Respiratory Tract. This section would be enhanced by including one of the well-known figures illustrating the gross structure of the respiratory tract.

Page 7-9: The chapter would be enhanced by inclusion of a figure illustrating regional deposition in the human as a function of particle size.

Page 7-24: The chapter would be enhanced by including one or more figures illustrating inter-species patterns of total deposition and regional deposition for commonly used laboratory animal species and the species of interest, humans.

Page 7-38: The chapter would be enhanced by including one or more figures illustrating inter-species patterns of clearance and retained burden for commonly used laboratory animal species and humans.

CHAPTER 8 - TOXICOLOGY – GENERAL COMMENTS

The introduction of the chapter could be strengthened with a better linkage to the epidemiology chapter. The epidemiology chapter relates findings from multiple studies showing an increase in health effects, primarily cardio-respiratory effects especially in susceptible populations associated with various PM indicators when assessed in larger populations (usually a study size of over 10,000 mortality or morbidity events times study days) with a relatively low prevalence rate for the adverse events of concern. Restating this at the beginning of the Toxicology chapter will help provide a setting for consideration of the toxicological findings on PM in humans and laboratory animals under controlled exposure conditions. In my opinion, the toxicological findings have generally not been very informative, as to how PM may be pathogenic in humans or in identifying specific putative causative agents with PM. I suggest that the lack of progress relates to the blunt "statistical" nature of current toxicological methods for tackling low probability of added effects when the diseases of concern have low prevalence rate outcomes even in susceptible populations.

It would also be useful if the introduction of the chapter could identify the challenge of moving beyond characterizing whether a specific material is hazardous; i.e., capable of causing adverse effects at any level of exposure, to the critical issue of the relevance of the findings at typical ambient concentrations of PM.

The section of the chapter addressing susceptible populations should briefly consider the issue of cigarette smoking as a risk factor. I submit that the vast majority of increased health effects associated with PM in adult populations are observed in smokers or former smokers. These populations contribute a disproportionate number of individuals with cardio-respiratory disease and, thus, are the major susceptible population at risk from PM-related disease. It is noteworthy that to date a well-defined animal model has not been found for cigarette smoking induced cardio-respiratory disease. Smoking-related diseases develop slowly and are usually manifested late in life. The absence of such models is also reflected in the lack of well-developed and validated models of the common PM-related cardio-respiratory diseases. The minimal nature of respiratory disease in young rats exposed for months to heavy doses of cigarette smoke may also help rationalize the relatively refractory nature of rats exposed for modest lengths of time to PM and constituents.

The section of Chapter 8 on in vitro exposures lacks information that would help place the in vitro studies in perspective relative to in vivo exposures of humans to ambient PM. In comments on Chapter 7, I noted the need for calculations of deposition rates and steady state burdens of PM in humans exposed to various levels of ambient PM. Such information presented in detail in Chapter 7 could be summarized in Chapter 8 and provide a metric for comparison to the levels used in in vitro studies. A review of these in vitro studies suggests that the concentrations of PM and constituents studied are orders of magnitude in excess of any concentrations likely to be

observed in humans at even the highest ambient concentrations encountered.

Chapter 8 also notes "there is growing toxicological evidence that diesel PM exacerbates the allergic response to inhaled antigens." (Summary statement pages 80-86, lines 17-180.) This statement and the supporting text needs to be qualified because of the high concentrations of diesel PM or extracts used. The last published EPA Health Assessment for Diesel Exhaust included a calculation of the quantity of diesel PM (and the organic fraction) inhaled and deposited. That calculation should be referenced in this document in both the chapter on dosimetry and in Chapter 8.

CHAPTER 9 - INTEGRATIVE SUMMARY – GENERAL COMMENTS

This chapter represents an excellent start toward providing an authoritative summary of current knowledge of PM. It could be improved with some signification additions. As noted earlier, the entire document from the introduction to this concluding chapter should build on the sources-health responses paradigm recommended to the NAS/NRC PM Committee.

Section 9.3 on ambient particulate matter could be enhanced by providing some summary data on past and current PM levels. This could include information from the latest EPA "Trends Report," the NMMAP study on 90 cities and the temporal trend for PM (as TSP) and other pollutants for Philadelphia (from Kelsall et al, [1997]).

Section 9.4 on human exposures needs to be augmented with Figure 2-18 (Clayton, et al, 1993) from the Staff Paper.

Section 9.5 needs to be augmented with information on deposition rates and steady state levels for various regions of the respiratory tract normalized to typical ambient PM concentrations.

I suggest that a portion of Section 9.7 on Risk Factors be moved up after the present Section 9.5. This new section, entitled "Baseline Health Statistics" could help set the stage for the present Section 9.6 on Health Effects.

This new section should include the present tables 9-9 and 9-10 and additional information on key health statistics. I suggest this include summary baseline data on inter-city variability from the NMMAP study for 90 cities. It should also illustrate temporal variability using the data for Philadelphia from Kelsall et al (1997).

At some point in the chapter it would be useful to include data, perhaps from the NMMAP study on effects estimates for other key pollutants (O_3, NO_2, SO_2, and CO), to help provide perspective for the PM effects estimates.

Chapter 9 is seriously deficient in not providing a well-developed section on ambient concentration-response relationships. This includes consideration of the threshold issue as well as the relationship between ambient concentration-response as natural background levels are approached. This is not merely a matter of thresholds versus linear responses.

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Chapter 7 Dosimetry of Particulate Matter

Overall, this chapter summarizes well what has been presented in previous EPA documents and gives additional useful new information. However, there are several rather dogmatic statements which are unsupported and need either to be referenced or to be labelled as speculative. Some sections are also rather simplistic by stating the obvious, a bit more depth would help. This review summarizes on a page-by-page basis some suggestions for changes, deletions, additions.

Page 7-7, line 7: In addition to defining the term "inhalability" it would also be useful to define "respirability" since later on there appears to be some confusion as to which term should be used.

Page 7-9, line 2: CMD is not necessary, it implies a size distribution whereas here the upper limit is meant.

Line 4: The Frampton *et al*. study had both male and female subjects.

Line 9: Add after "diameter" the sentence: There was no gender difference.

Line 10: A statement could be added that this result compares favorably with the ICRP 1994 model.

Line 13: A sentence should be added here listing some of the values of the Jaques and Kim study, rather than giving the results only in relative terms.

Line 24: A sentence should be added here stating that at the same time, there is a shift in deposition sites from more peripheral to central or extrathoracic regions.

Page 7-11, lines 18-20: 94 - 99 percent is not consistent with the result reported in the previous paragraph (Yu *et al*.) where only 54% deposition was found for 1 nm particles, and these have the highest deposition efficiency.

Page 7-12, lines 7-11: The efficiency of the nose as a filter for ultrafine particles has to be seen in the context of the size within the ultrafine range. Whereas it can be very high for nanoparticles below 10 nm, the filtering capacity becomes less for ultrafine particles of 20 nm and greater.

Page 7-14, lines 10: Change "fine" to "ultrafine". In this paragraph again it would be helpful to give some of the values that were found by Kim and Jacques in their studies in terms of deposition efficiencies. A statement comparing their results with the ICRP model would also be helpful, for example, the total deposition in the alveolar region found by Kim and Jacques for 40 and 60 nm particles of ~33 and ~27 percent, respectively, are in excellent agreement with the ICRP model.

Line 30: To understand the modeling result it would be helpful to provide data on the size distribution of the environmental aerosols in terms of MMADs and geometric standard deviations.

Page 7-15, line 1: What kind of mathematical model was used? A brief descriptor would be helpful.

Lines 4-6: If 36 of the inhaled coarse particles were deposited in the lung, that doesn't add up if only 4 percent were in the tracheobronchial region and 2 percent in the alveolar region. Please check. Likewise, 9 percent of the fine particles deposited in the lung is not explained by 6 percent in the alveolar and a small fraction in the tracheobronchial region.

Lines 13-14: Here again 18 percent deposition in the lung is not explained by 2 percent in tracheobronchial and 3 percent in alveolar regions.

Line 23: I assume the cautionary note refers to the numbers (10^3, 10^5, *etc*.) but the general trend of differences between coarse and fine particle surface area and cell doses can also be derived from other models, *i.e*., ICRP, MPP Dep model.

Page 7-17, lines 24-26: I suggest to add here also that exercising will cause a shift in deposition sites from peripheral to more central airways as had been modeled by Martonen.

Page 7-18, lines 2: When differences in deposition between females and males are described here, these results as well as those from other studies comparing the gender-related deposition efficiencies should be critically evaluated: Both men and women breathed at the

same tidal volume of 500 mL at 15 breaths/min, and this means for women, generally smaller than men, an increased minute ventilation compared to their normal breathing condition. Therefore, gender-related differences in deposition found here may be due to the fact that women breathed at a relative larger minute ventilation and would not show if both men and women would breath at their normal size-adjusted tidal volumes. A critical discussion along this line should be added.

Line 13: It would be helpful to add here a summarizing paragraph since the reviewed studies on gender differences show somewhat differing results and it would be appropriate to have a summarizing concluding statement.

Page 7-20, lines 1-2: When comparing deposition efficiencies in the lungs of children *vs*. adults, it should also be considered that children have a higher minute ventilation per unit body weight compared to adults.

Line 26: Again, a summarizing paragraph would be helpful regarding age-related deposition differences.

Page 7-25, line 17: ">5 µm" should be "<5 µm" since it is this lower range where inhalability plays a role in deposition differences between rats and humans. Above 5 µm particle size inhalability is no issue for rats as far as the lower respiratory tract deposition is concerned. It would, however, be useful here to also discuss the importance of differences between rats and humans with respect to respirability of particles, since differences here are more pronounced: Particles >5 µm aerodynamic diameter are still well respirable in humans, but not in rats.

Page 7-26, lines 14-24: These model calculations by Hofmann and colleagues are not easily understandable. For example, the statement that alveolar deposition in humans was lower than in rats over the size range of 1 nm to 10 µm raises the question as to whether 10 µm particles at all will reach the alveolar region in the rat? This is clearly beyond the respirability range for rats. Did the model by Hofmann *et al*. consider the nasal filter in rats, or was it based on particles entering the trachea? This needs some clarification. In addition, when comparing deposition efficiencies between rats and humans, it should be mentioned here that to compare the deposited fraction alone is not enough: What one needs to also compare is the deposited amount per surface area which can give a quite different picture.

Page 7-27, line 8: Again, it is surprising that particle size-dependent deposition is qualitatively similar in rats and humans for particles up to 10 µm, see comment on respirability above.

Page 7-28, lines 3-14: This paragraph does not belong here, it is not dealing with deposition but with retention pattern after chronic exposure to particles in rats and non-human primates. In line 9 of this paragraph the term "deposition" should be replaced with "retention". The whole paragraph should be moved to a later section where retention is addressed.

Lines 15-22: In lines 19 and 22, differences between rats and humans are addressed without saying in which direction these differences go. This should be made clearer. Moreover, this paragraph is rather vague, it needs to be a summarizing paragraph to point out the major differences between rats and humans in a succinct way. The results by Hofmann *et al*. summarized above are not easy to understand, and they certainly require a concluding, clarifying summary.

Lines 23-31: This paragraph is a bit simplistic, and seems to have been written in a hurry. I suggest in line 25 to replace "dose response" with "retention". In line 27, how is the dose affected by species sensitivity? When different dosemetrics are addressed here in lines 28-31, then all of them should be mentioned, *i.e*., number of particles, surface area of particles (there are several studies showing the importance of particle surface area), the mass of particles as well as the volume of particles. The dosemetric in terms of particle number *vs*. mass, etc., depends also on the physico-chemical characteristic of the particle, *e.g*., for soluble particles the mass is probably still the more important parameter whereas any of the other parameters being more important for poorly soluble particles. It is also not clear what is meant in line 30 with the term "deposition": Is it deposition in terms of fractional deposition, deposition in terms of mass? The deposition density in the rat is not necessarily higher than in humans because of the smaller surface area of the rat lung, it depends very much on particle size and fractional deposition

efficiencies as well as the ratio of rat to human lung surface areas. This paragraph needs to be revised.

Page 7-29, lines 1 and 2: This concluding sentence stating that deposition density should be considered when extrapolating health effects seen in rodent studies to the human situation needs to be expanded in that other factors should be considered as well, such as dose in the specific region, dose per unit surface area, dose per cell (*e.g*., alveolar macrophage), and also particle parameters such as solubility, volume, surface area, size. Although deposition density is very important, other factors should not be neglected.

In this section on interspecies differences, it would also be useful to mention the availability of the Multiple Path Particle Deposition model (MPPDep) which allows the calculation of particle deposition in human and rat respiratory tracts assuming different exposure scenarios and breathing patterns and particle parameters.

In general, in this section on particle deposition efficiencies in the human respiratory tract and in the rat, a figure would be useful so the reader would not have to consult other publications for this purpose.

Page 7-31, Figure 7-3: If the size of the arrows in this figure indicates major *vs*. minor clearance pathways, then the arrow from phagocytosis by alveolar macrophages to passage through alveolar epithelium should clearly be a minor arrow since only a tiny fraction phagocytosed by macrophages takes this route (studies by Harmsen *et al*.), and the existence of this route might even be questioned. However, under particle overload conditions the translocation to interstitial sites *via* endocytosis by type I and type II alveolar cells becomes a major pathway, but this does not occur *via* particle-laden alveolar macrophages.

The meaning of the double-headed arrow from pulmonary capillary endothelium to phagocytosis by interstitial macrophages is not clear, does it mean that particles or interstitial macrophages with particles are coming back from the endothelium? Also, the arrow from phagocytosis by interstitial macrophages to pulmonary capillary endothelium is not clear: Is there compelling evidence that, indeed, interstitial macrophages with phagocytized particles are entering the pulmonary capillary endothelium?

Page 7-32, line 3: Not all solutes will be absorbed rapidly, it depends on the rate of dissolution from a particle as well as on the molecular size of the solute and other parameters to be discussed later.

Line 10: Probably meant here is that particles re-enter the airway lumen from mucosal sites, is there any reference for that?

Line 23 and 27: I don't think that the general statement can be made that the "magnitude of any increase in cell number (alveolar macrophages) is related to the number of deposited particles rather than to total deposition by weight". This would result in a huge increase in the case of deposition of ultrafine particles. Furthermore, cytotoxicity of a given particle is certainly a big stimulus for inflammatory cell increase, and if particles are soluble then the mass and not the number is the major determinant for eliciting cells. A better dosemetric to relate cellular responses to deposited poorly soluble particles would be particle surface area, and there are a number of studies which demonstrated that specifically for ultrafine and fine particles - given that they are not chemically different - particle surface area correlates very well with the increase in inflammatory cell numbers. Again, that applies only to poorly soluble particles and not for soluble ones where mass is the more appropriate dosemetric.

Page 7-32, line 31: This describes the pathway in Figure 7-3 of macrophages traversing the alveolar capillary endothelium directly entering the blood stream. Again, has this been demonstrated for macrophages with phagocytized particles?

Page 7-33, lines 1-11: There are a number of statements in this paragraph which need to be supported by appropriate references. For example, what is the evidence for macrophages with phagocytized particles traveling to extrapulmonary organs? Are these new data? What is the evidence of particles binding to macromolecules?

Lines 17-29: The clearance of solutes is a bit superficially treated here, it is not that simple. It depends on the lipophilicity *vs*. hydrophilicity of solutes and the molecular weight. There are also different solubilities depending on the intra- *vs*. extra-cellular localization

of particles due to respective changes in local pH. After dissolution or leaching of some components from a particle these can be binding of solutes (metals) to macromolecules; an important pathway also is transport *via caveolae* across the epithelium as well as the endothelium. The importance of differences between epithelial *vs*. endothelial pore sizes for lower molecular weight solutes could also be addressed here.

Page 7-38, line 1: Snipes and Clem used 3, 9, and 15 µm particles and found only the 3 µm to be translocated, did Takahashi really see 5 and 9 µm particles being translocated?

Lines 4-6: One has to be very careful when drawing conclusions with respect to lymphatic transport of particles based on intratracheal instillation studies: In such studies high doses are instilled as a bolus leading to local overload which messes up the normal clearance significantly and easily can result in lymphatic translocation which will not occur under normal conditions. Also the statement that particles >5 µm have significant deposition within the alveolar region is not correct for the rat. In the context of species differences related to lymphatic clearance, studies by Thomas *et al*. (1971) could be cited here showing differences between rodents and dogs, accumulation of particles in local lymph nodes being much greater in dogs.

Page 7-42, line 29: A most important feature of Morrow's hypothesis is that a volumetric overloading of alveolar macrophages occurs which eventually impairs its clearance function.

Page 7-43, line 11: I am not sure I understand why the slower alveolar macrophage-mediated clearance in humans compared to rats (it is always slower in humans) would cloud the overload relevance for humans: Humans also live about 25 times longer than rats.

Lines 14-15: It is hard to imagine how under normal environmental exposure conditions, overload will occur in compromised lungs. What compromised lungs would that be?

Line 26: Although it is generally assumed that intratracheal instillation delivers an "exact" dose to the lung, this does not mean that this dose is really found there shortly after the instillation because some of the material is rapidly cleared out by the following exhalations. The amount of this loss depends highly on the instilled volume as well as the instillation technique, *i.e*., synchronizing with respiration or not.

Page 7-44, line 9: It is not clear what is said here, the amount that is deposited in the lower airways by instillation can be adjusted, it is not due to by-passing the nose. Probably what is meant is that the distribution of material is different between the two techniques.

Page 7-45, line 11: It is unclear what is meant by percentage retention of particles: Is that the intercept of the retention curve with the ordinate, or is that the retention halftime? If the retention halftime is meant here that would be explainable since normally by instillation high doses are delivered which result in overloaded areas with retarded clearance. Thus, it might be better to compare inhalation and instillation-associated retention kinetics by describing the respective retention halftimes.

Line 18: The bulk of the instilled material certainly goes beyond the terminal bronchioles, otherwise you would see all of it being cleared in a short time by the mucociliary escalator. Of course, the very periphery of the lung is not well dosed, and as mentioned before, the coverage depends also on the instillation technique, *i.e*., synchronization with breathing or not.

Line 29: Disposition of particles is only one factor determining their biological effects.

Page 7-50, line 1-6: For a discussion of "human equivalent concentration (HEC)" EPA's RfC document should also be quoted here. Furthermore, earlier in this section, emphasis was on the lung burden expressed as per unit lung surface area as being more appropriate, whereas here the amount per gram of lung is indicated. This might be confusing for the reader.

Lines 13-19: The Asgharian 2000 reference is missing in the reference list, is that a publication describing the MPPDep model which should be mentioned here as well?

As a general comment on this section, it should also be stated in a concluding summarizing paragraph that all models are just that: models. They have inherent uncertainties, which can be large and differences between model results can probably most of the time be explained by these uncertainties.

The title of this section is also somewhat misleading, both 7.6.1 and 7.6.2 deal with deposition and some clearance and retention, but the disposition of particles in terms of where particles move after deposition is not really addressed in this section on "Modeling of disposition". Much of what is reviewed in this section is already described in prior sections of this document and somewhat redundant.

Page 7-52, line 25-31: As we had discussed in the previous review, one has to be careful with the interpretation of the results by Nikula *et al*. (1997) since it was derived from a one timepoint post-exposure evaluation only: Rats with particle overload clear significant amounts to the regional lymph nodes, which means that the particles have to become interstitialized first; once in the interstitium, the rate of interstitial clearance to the lymph nodes may be much faster in rats than in primates which cannot be evaluated from a result obtained from one timepoint only. At this one timepoint, the interstitium in the rat could already be significantly cleared which would incorrectly be interpreted as less interstitialization. Therefore, whether this reflects truly a difference in retention pattern between rats and primates or a difference in interstitial clearance rate cannot be decided from the analysis at one timepoint.

Chapter 8

Page 8-1, lines 5-10: Among the questions listed here should also be the most important one, namely: Does PM at relevant ambient concentrations cause adverse effects?

Line 15: Change "air" to "PM". Add at the end of the sentence in line 16: "or suspension".

Page 8-6, lines 16-17: The study by Kuschner *et al*. used median concentrations of 133 mg/m^3, at which concentrations the particles are no longer ultrafines, so one has to be careful with their conclusion that there is no difference between fine and ultrafine particles. There is no question that chemical composition, surface radicals, *etc*., play a role as well, which is not disputed, just think about ultrafine PTFE *vs*. ultrafine TiO_2. But to exclude size as an important factor for toxicity is wrong. This comment has already been made by me for the previous criteria document and obviously was not considered.

Page 8-7 and 8-8, Studies by Osier: The inhaled concentration for the TiO_2 was 125 mg/m^3 for 2 hrs. (not µg) in order to match the intratracheally instilled dose in terms of pulmonary deposition.

Page 8-9, lines 19-22: The dose of 5 mg deposited in the human lung in this study is certainly much more than can be deposited from ambient air.

Page 8-10, line 18: Change "Teflon polymer" to "PTFE".

Lines 22-23: Again, the study by Kuschner *et al*. is cited here as demonstrating that composition and not particle size was responsible for health effects in this study. Given that the median concentration of the particles was 133 mg/m^3, these particles were no longer ultrafines, but aggregates. Obviously, in addition to size, composition is also a very important parameter and both need to be considered (see above).

Page 8-19, line 30: It would be useful to point out in this context that in general the intratracheally instillation studies failed to include a benign particle such as TiO_2 as a comparison to show that the effects observed are more than just a general particle effect.

Page 8-22, line 24: I strongly suggest to include the word "high" when the ROFA doses are addressed.

Page 8-23, line 30: The dose of LPS is given here as 5 or 50 µg. Is that the inhaled dose? Is that the dose in the nebulizer, or an estimated deposited dose in the lung?

Page 8-24, Study by Elder *et al.*: The concentration of 100 $\mu g/m^3$ is for the particles, not for LPS.

Page 8-30, lines 3-5: The effects observed here with ROFA inhalation should be viewed in the context that the inhaled concentration was 15 mg/m^3 and that inspite of this high concentration there were much lower or no effects compared to instilled ROFA which caused increased mortality.

Page 8-31, line 6: The concentrations of ROFA given were not only high, I suggest to describe them as "very high".

Line 19: Was the change in heart rate variability an increase rather than a decrease? I think what should be stated here is that the ratio of low and high frequency band of HRV decreased.

Page 8-32, lines 10-19: Here the two different dog studies by Godleski and Muggenberg are compared, however, the studies are significantly different from each other in that Godleski used CAPS and Muggenberg used ROFA, the particle size might also have been very different. Thus, it is difficult to compare the different findings between the two studies given also that storage of ROFA could have played an important role in altering its toxicity. It should also be considered that the dogs in the study by Godleski were exposed *via* a tracheostomy tube.

Page 8-34, line 4: I suggest to change "high concentrations" to "only high concentrations."

Page 8-37, lines 28-29: The exposure concentration of ROFA was 15 mg/m^3?

Page 8-38, line 17: Change "Teflon particles" to "ultrafine PTFE fumes".

Page 8-39, line 9: In this section of age-related differences in PM effects, the studies by Elder *et al*. should be included, they describe effects of inhaled carbonaceous model particles in LPS-sensitized rats of old and young age (Elder, A.C.P., Gelein, Finkelstein, J.N., Cox, C. and Oberdörster, G. Pulmonary inflammatory response to inhaled ultrafine particles is modified by age, ozone exposure, and bacterial toxin. *Inhalation Toxicology* **12** (Suppl. 4): 227-246, 2000; Elder, A.C.P., Gelein, R., Finkelstein, J.N., Cox, C. and Oberdörster, G. Endotoxin priming affects the lung response to ultrafine particles and ozone in young and old rats. Inhalation Toxicology 12 (Suppl.): 85-98, 2000).

Page 8-40, line 2: Is a fibrotic response an important endpoint for ambient PM?

Page 8-39 thru 8-45: In this section on genetic susceptibility to inhaled particles, a discussion on the dose levels used in the different types of studies would be useful to put them in perspective to ambient levels and deposited doses.

Page 8-48, lines 7-9: Among the severe limitations of *in vitro* studies are the dose levels which are generally orders of magnitude higher than experienced *in vivo*; and in addition the fact that only acute effects and mechanisms can be evaluated *in vitro* which could be very different from mechanisms causing chronic effects *in vivo*. These significant limitations should be added onto the discussion in this section.

The title of **Chapter 8.5** refers only to *in vitro* exposures, which gives the impression that mechanisms can only be evaluated by doing *in vitro* studies. This is not correct, mechanisms are also evaluated by *in vivo* studies, in fact, the *in vivo* studies may be more important since they only can provide compelling evidence that any mechanistic pathway explored *in vitro*, indeed, is also operating under *in vivo* conditions which are obviously much more complex.

Page 8-57, lines 30-31: This two-line summary can be used for any type of particle and is not very specific, and it may be useful here to also again point out that the high doses that are used in these *in vitro* studies need to be considered. A sentence stating that detailed specific mechanisms related to ambient PM still need to be uncovered should be included here.

Page 8-65, line 8: What does the study of i.p. injection of ROFA contribute to an evaluation of mechanisms? This study doesn't seem to make much sense.

Lines 18-30: When comparing different dust materials in *in vitro* studies, it becomes very difficult to rank the toxicity of the different dusts because it is not known as to whether the different particles are internalized by the cells to the same degree, and also the dosemetric in terms of mass *vs*. particle number or size can significantly influence the result. The term "exposure–dose" used in line 30 is not clear, what does it mean?

Page 8-70, lines 15-16: This statement is only true if the chemical composition of the ultrafine particle and larger particle is the same, which should be added here.

Lines 15-29: Lines 27 – 29 provide an explanation for the observation that high doses of fine particles cause a greater effect than high doses of instilled ultrafine particles. Indeed, results of our earlier study (Oberdörster *et al*., 1992) demonstrated that the significant amount of ultrafine particles being interstitialized when high doses are instilled causes a decrease in the inflammatory cells in the alveolar space compared to inflammatory cell influx at lower doses of instilled ultrafine particles.

Line 31: The studies by Oberdörster *et al*. (2000), which are alluded to here, in

old and young rats and mice used only ultrafine carbon particles, see also the publications by Elder *et al*. (2000, 2001) which were mentioned earlier in my comments.

Page 8-72, line 11: Replace "properties" with "area".

Page 8-73, lines 5-8: One has to be careful to characterize ambient PM as ROFA which has been used in a number of animal and *in vitro* studies. The ROFA that was used was collected from a bag house, and – as was pointed out earlier in this document – has a different metal content than the fly ash which is actually released into the environment, also metal solubilities are different. Furthermore, the high doses that were used in the ROFA studies need to be mentioned here as well.

Page 8-74, Section 8.5.5.2: This section reiterates studies that have been described before in this document. It should be remembered that the studies which are used here to demonstrate a specific mechanism to cause systemic effects have been run at very high doses or exposure concentrations, and thus, one needs to be very cautious to extrapolate these responses to relevant ambient concentrations of PM. What the studies do is show that the concept of a specific pathway or mechanism is valid in principle, but this needs to be validated and verified by additional studies using relevant exposures.

Page 8-81, line 26: Include (Elder *et al.*, 2001).

Page 8-83, Section 8.7 Summary: This section provides a good summary of our present state of knowledge. There should be a few clarifications:

Page 8-85, line 14: Implications for what? The implication I see here is to conduct further studies on the importance of metals, and that the ROFA studies have pointed out the importance of the metal concept for PM toxicity in general.

Page 8-87, line 16: Another ultrafine ambient PM concentrator was developed by Koutrakis and colleagues.

Section 8.7.1.2, Susceptibility: Among the susceptibility factors, not only genetically or induced compromised health should be listed but also age as a factor.

Robert Rowe, PhD

Below are revised comments on the second draft CD and draft Staff Paper for the PM NAAQS. The EPA staff are to be commended for the work to date, especially recognizing the significant growth in literature relevant to the PM standard. My comments focus on economic and visibility perception portions of the materials provided.

Visibility Impairment Assessment

The Staff Paper Section 5.2.5, and a supplemental paper, address a proposed approach to address visibility impairment in terms of human judgement. I encourage EPA to pursue this perceptions, preference and economic valuation work as important to setting the secondary standard. However the work completed to date should be seen as being only very preliminary. It is important that a more comprehensive workplan be developed, including how the results may be used as input to decisions about the secondary national standard, and that the type and level of work effort be consistent with the expected use of the work.

My key recommendations are that:

1. EPA should conduct several additional focus groups in the Washington, D.C. area to address basic issues in the research.
2. EPA should then conduct similar preliminary analyses in another city that is diverse from Washington, D.C.
3. Based on the above, EPA should develop a more comprehensive workplan on the issues and objectives, data to be collected and its uses, steps to be performed, survey instruments, and time schedule. I recommend a peer review at this stage.
4. EPA should develop a plan that will provide a sound sampling strategy, and not just one or two focus groups in a variety of locations. This may require OMB approval.

Below are additional detailed comments on the visibility focus group materials.

- Little confidence should be attributed to one focus group of 9 people in one location (Washington, D.C), and this group should not be seen as sufficient to launch a multi-city assessment. I advise repeated groups in the first location to obtain more data and to address issues before proceeding to other locations, or to conclusions. Among the issues that could be considered are (1) how do the types and kinds of locations presented in the vistas alter the conclusions, if at all? (2) how much are perceived health concerns affecting the judgements, and how can this be better addressed? (3) what does it means when people say the impairment is acceptable or unacceptable? It is based on the view, the impact on their mood, are there behavioral changes? Does this mean the identified threshold level is acceptable every day or several days a year? Does this mean respondents are no longer impacted, or just that they think the likely perceived costs of further control may not be worth it (and on what basis do they make such a judgement), or that further improvements are not realistic. In this rating, respondents are participating in a stated preference (SP) assessment, and more attention should be given to the SP literature. (4) Which measure will be used? For example, in the simple rating, the cross over point for unacceptable is 20 : g/m^3, but with the "how many hours a day" rating, 32.5 : g/m^3 is acceptable for as many as 4 hours a day by two-thirds of the respondents (and thus presumably a level of higher than 32 : g/m^3 for 4 hours a day would be acceptably on a simple 50% rule), and based on the economics data, there is clear impairment below 20 : g/m^3.
- When moving to multiple locations, issues arise such as which vistas to present, what type of impairment (which varies in some locations), and how correlated will the ratings across locations be to existing conditions across locations (valuation literature would suggest status quo bias leading to anchoring and some adjustment to improved conditions).

- While the approach follows similar work at the state and local level, it is not clear that the approach is sufficiently resolved for a national standard when the "impairment" threshold may be highly variable across locations. How does EPA see using the results? How might the results tie in to the PM NAAQS or other visibility rules?

- The economic valuation questions are preliminary, yet highlight there may be meaningful losses at visibility levels below the 50% rule for acceptable ratings. In the preliminary focus group the switch from 50% acceptable to 50% unacceptable occurs at 20 : g/m^3. However, when provided a choice, 5 of 9 would choose 15 : g/m^3 and pay $50/year, as opposed to 22.5 : g/m^3 and paying $10/year (2 were indifferent between 15 : g/m^3 and 22.5 : g/m^3, and 2 chose 22.5 : g/m^3 over the status quo of 32.5 : g/m^3). This suggests a significant value for visibility conditions below the 50% rule level for either the simple ratings or hours per day ratings. I support further investigation into the economic valuation approach, with much more attention to survey design consistent with the stated preference valuation literature. To address the joint product issue between visibility and health, one might revisit the Carson et al. Cincinnati work performed for EPRI some years ago, which by the way showed losses down to just a few days a year of visibility impairment (e.g., an indistinguishable change when presented on an annual average basis).

- There are important concerns with the proposed "focus group" approach to this assessment. Generally a study consisting of a group of focus groups across different locations may not be viewed as sufficiently rigorous for the intended policy application. EPA should see the focus group approach only as a preliminary effort to a larger scale survey effort.

Staff Paper Visibility Section

This section is better than the corresponding section in the CD. The two sections should be consistent. A few suggested editorial changes for the Staff paper (aside from continuing to include but reduce the discussion of this work). On page 5-16, I recommend active use and

passive use values as opposed to use and non-use, to better identify that in some cases visibility is actively enjoyed, while in other cases it is passively enjoyed, and realize that it is often difficult to separate benefits by these categories (e.g., where does option value fall?). Page 5-23 of the staff paper was missing.

Criteria Document Chapter 4: Environmental Effects

General Notes Overall, this section is reasonably comprehensive. Two overriding considerations are (1) can the presentation be more focused to key questions in the setting of standards, rather than a litany of information and appendicies (this seems particularly true for the global climate sections), and (2) can economics, if it is to be addressed at all, be addressed more consistency in the various subsections.

Section 4.2.2: Natural Ecosystems

- Lines 7 through 15. I recommend some terminology clean-up here, rather than propogating terms inconsistent with the broader resource economics literature. All benefits from ecosystems can be described as ecosystem services. I think this could use revision, especially on page 4-20, to state something along the lines of "there are a wide range of ecosystem services, including (1) some with readily recognized market value (e.g., fish, timber, minerals,…) and (2) others services without current or readily identified market values. For the purposes of this discussion only, we refer to the first group as "market services" or "goods" and the second as "non-market services". Table 4.2 illustrates various market and non-market services provided by ecosystems…" Then, I think Table 4-6 is much more informative than Table 4-2 and could replace Table 4-2.

- Page 4-83 identifies economic literature to demonstrate the significance of ecologic resources and services to mankind (Pimentel and Costanza). These numbers are presented, perhaps, with too much credence. There is significant controversy in the economics literature about the reliability of the specific estimates (See the Special Issue of Ecologic Economics, April 1998, and Freeman, 1999), not the least of which is that economics is much better suited to evaluate individual services, or better yet changes in service flows for an individual ecologic service, than it is to evaluate the total value of all ecologic services. Economics aside, most all agree that ecologic services are central to human life and obviously of substantial value. Consequently, substantive impact on ecologic services have the potential to have an important impact on human welfare.

Section 4.3.9 Visibility Economics. Generally, there should be more consistency to the Staff Paper write-up. To the degree this is retained along its current lines, I note the following edits.

- Page 4-111 line 27. Replace "costs" with "losses" (here and generally throughout the section).

- Page 4-111, line 29, replace "cost/benefits" with "losses from visibility impairment".

- Page 4-111 line 31, and continuing to page 4-113, line 3. The avoided cost method, while used as a market cost measure of materials damage, and sometimes in other application, is not used in the visibility literature and should not even be discussed here. Just start with something similar to line 4 "There are several methods…."

- Page 4-113, line 12, it would be useful to have a citation on visibility property value studies (e.g., Chestnut and Dennis, or the NAPAP work from a few years earlier for summaries, which is cited elsewhere in the CD and staff paper). There is quite a bit of property value literature, with the difficulty of sorting out value differences into visibility and health components. One could also cite some of the new property value applications (Thayer and Murdoch).

- Page 4-113, lines 13 through 19 focuses on CVM, but really is about stated preference methods, including CVM applications. Some of the past economic studies are more like SP choice studies than conventional CVM applications. Consequently, it may be appropriate to merge the paragraphs starting on lines 13 and 20.

- Page 4-113, line 19 could use a citation, either NAPAP or Chestnut and Dennis, or Mitchell and Carson.

- Does the Hanley and Spash reference discuss visibility applications in specific and in detail?

- Page 4-113, line 31. "Davis" should be "Dennis".

Health Risk Assessment (Staff paper Chapter 4 and separate paper).
- I support conducting the assessment in more than 2 locations, as discussed at the meeting.

- Staff paper 4-13, lines 10-26 discusses assumptions about changes in ambient conditions to meet standards, relying predominately on the rollback method. Using the rollback method is reasonable, but EPA should give careful attention to the proposed sensitivity analysis of alternative adjustments (lines 24-26). With increasing costs of compliance, episodic and other control strategies that reduce the highest concentrations may receive increased attention. Further, given that the population exposed is not uniform across concentration levels, and many concentration-response functions are non-linear, differences in the assumptions to reduce concentrations to achieve standards can have a significant impact on the risk assessment.

- Deck et al, 2001 is cited several times, starting in the first paragraph, but is not available. It may be useful to provide this paper for this review.

Criteria Document Chapter 9

This chapter is well done as a series of separate summaries, but it needs more integration and needs to be reduced in length – not everything needs to be summarized. It appropriately focuses on the larger questions of increasing consistency in the results of available health effects literature and extensions to this literature. In terms of the important question of retaining or revising the existing $PM_{2.5}$ standard levels (15 ug/m3 annual average and 65 ug/m3 24 hours), little is presented in this chapter on the strength of the evidence, shapes of the estimated C-R functions around these levels, or effect thresholds (although this is touched on in Section 6.4.6).

Jonathan Samet, MD

Chapter 5 - General Comments:
In general, this is a cohesive and thorough chapter that carefully sets out concepts of exposure assessment, measurement approaches, and findings. The literature review appears complete and findings are well represented in tables and in the text. The chapter has a potentially key role in setting a framework for interpreting the epidemiological data presented in Chapter 6. The chapter does address the implications of the exposure literature for interpreting the epidemiological evidence. Unfortunately, there is little linkage between the two chapters in this regard; Chapter 6 almost reads as though Chapter 5 had not preceded it. There is a need for better integration, a burden which clearly lies with the authors of Chapter 6.

This chapter also discusses issues related to confounding and measurement error that overlap with Chapter 6. With regard to issues of confounding, it will be important to have a uniform view throughout the CD. My comments for Chapter 6 should be considered in this regard.

Specific Comments:
Page 5-19, lines 15-18: Generalizability (external validity) is not dealt with well here. A "purposeful study" may give generalizable information; the extent of generalizability is a matter of judgment, based on study participant characteristics. The term statistical inference is used inappropriately here.

Page 5-41, lines 5-16: This paragraph is far too sweeping in its condemnation of the exposure assessment literature. What are the "important questions" that are so poorly answered.

Chapter 6 - General Comments:
This lengthy chapter provides an exhaustive, descriptive summary of the most recent epidemiological findings on particulate matter and morbidity and mortality. The literature review is comprehensive and the tables offer useful summaries of an extensive literature. There are, however, weaknesses that should be addressed; these weaknesses may reflect the multi-authored nature of the chapter which has resulted in an uneven approach in style, synthesis, and interpretation. Key aspects of the chapter needing to be addressed include:

1. The chapter is not adequately connected to the remainder of the CD. There is a lack of integration with Chapter 5, which should provide a foundation for exposure considerations related to interpretation of the epidemiological literature. This foundation is not used, and far less strong and competent text is provided.

2. The chapter fails to sharply set out key concepts—confounding, causal associations, and causal pathways, in particular. Effect modification is also not handled well and the text related to these key aspects of interpretation is often murky. In the chapter's introduction, it would be useful to provide diagrams indicating the relationships that hold under confounding, direct causal pathways, and indirect causal pathways. I have attached one possible set of diagrams. Additionally considerations as to confounding, reflect biological understanding as to the independent action of the confounder and not just patterns of association in data. Changes in estimates are not a particularly useful gauge as to the presence of confounding in the presence of measurement error, possible effect modification, and correlations among the independent variables. The text in places offers some clear thinking on these difficult topics, but much of it is not clear.

3. In interpreting data, there is excessive reliance on p values and attaining statistical significance for effect estimates. This needs to be corrected; the p value should not be held as a decision-making tool for data interpretation, as in the present chapter (see *Epidemiology* for a recent set of perspectives on this issue. Emphasis should be placed instead on precision of effect estimates (i.e., width of confidence intervals..

4. In fact, the chapter never clearly sets out how data will be interpreted. Summary judgments are offered but without reference to any common framework Judgments are often couched subjectively and there is a general failure to place the epidemiological evidence within the broader context of toxicological and dosimetric understanding. The framework for interpretation is badly needed. Throughout the text, there is variably use of significance level, precision of effect estimates, and magnitude of effect, as the effects of PM are weighed against those of other pollutants. The same problem is evident when the chapter interprets the literature on particle characteristics and components.

Specific Comments
Page 6-2, lines 11-15: This proposed hierarchy of "inferential strength" is neither correct nor useful.

Page 6-3, lines 19-21: This type of sweeping statement should be avoided. On close reading, the sentence offers only a garbled pejorative comment.

Page 6-3, lines 24-25: Around this point, the text needs to be very clear on causal and non-causal pathways. Also, the term "effect" and not "effects" modification is in general usage.

Page 6-4, lines 6-13: An example of muddled text around the confounding/causality issue. Lines 21-25, also exemplify this problem.

Page 6-9, lines 8-11: A not well developed fragment on measurement error that addresses its consequences for effect estimates and for confounding. The second clause of the sentence raises the complex issue of differential measurement error across independent variables with little explanation.

Page 6-49, Section 6.2.2.4: This section initially needs to set out issues that arise in interpreting the evidence on particulate matter components. Unfortunately, this has not been done well by the authors of many of the reports and the authors of this report fall into some of the same traps, particularly reliance on the p value (see, page 6-54, lines 1-8, for example).

Page 6-55, lines 25-30: These comments about PM2.5 sources need to be referenced.

Page 6-77, lines 1-5: Another example of very confused interpretation.

Page 6-96, lines 13-19: Basis of judgment not clear. Last sentence of paragraph needs clarification.

Page 6-101, lines 1-16: Too speculative.

Page 6-136, lines 20-22: The statement concerning barometric pressure is far too strong, based on a single study.

Page 6-126, lines 10-11: Multicity studies provide far more strengths than precision alone.

Page 6-217, lines 6-10: This sentence reads as though we have no prior knowledge on PM and health and should give equal weight to all models. That is hardly the case.

Pages 6-217-218: The sweeping generalizations about modeling need to be toned down. This is not the state-of-art.

Page 6-219, lines7-22: The discussion of lag structure, largely turning to statistical grounds for choosing the appropriate lag, is off the mark. Certainly, we have some knowledge of the kinetics of injury and substantial prior modeling work.

Page 6-225, lines 20-23: The conclusion may be correct, but its basis is not clear. The last sentence is not clear.

Pages 6-226-6-227: This section would be much stronger with my suggested addition.

Page 6-239, lines 21-27: There is little basis to assume different relationships across locations.

Page 266, lines 11-15: This paragraph shows little understanding of how evidence is assessed to determine causality of associations. What are "causal studies" from other disciplines.

Page 266, line 20-22: What is meaningful heterogeneity?

Page 6-269, lines15-23: What is the careful evaluation that is needed? APHEA and NMMAPS have been rigorously reviewed.

Chapter 9 - General Comments

This chapter is offered with the general and needed purpose of providing an "integration of key information". Unfortunately, it falls far short on this purpose, reading more as a summary, with interspersed comments and indications of research gaps. Even these comments, are not particularly penetrating. See, for example, lines 22-30, page 9-36, which overviews some issues in interpreting the epidemiological evidence. A higher level of analysis should be adhered to, particularly given the sophistication of the discussion since the last CD with regard to interpretation of the epidemiological data.

One approach that could be taken in this chapter would be to follow the NRC Committee's framework and to provide an "across the box" linking of what is known. The framework could also be used to highlight what is known and the uncertainties, as well as systematically point to research needs. This might be an appropriate way to conclude the chapter.

Follow-up Comments

These comments are intended to supplement the peer-review comments submitted in advance of the July 23-24, 2001, meeting of the Clean Air Scientific Advisory Committee (CASAC). These comments are based on my spoken remarks concerning interpretation of the epidemiological evidence in Chapter 6. Copies of transparencies used as the basis for these remarks are attached.

My remarks strongly urged rigorous and standardized use of epidemiologic terminology and concepts throughout the Criteria Document, particularly in Chapter 6. The Criteria Document needs to define and then uniformly apply the concepts of confounding and effect modification. As noted on the first transparency, confounding arises when a factor, associated in its own right with the outcome of interest, is also associated with the exposure under investigation. In this circumstance, a spurious association may arise between the exposure and outcome because of the confounding factor. For a variable to be a "confounder" in a particular data set, two conditions must be met: 1) the confounder needs to be associated with the outcome factor independently (i.e., it is a risk factor for the outcome); and 2) the confounding factor is associated with the exposure of interest in the data under consideration. A distinction should be made between a confounding factor and a "potential" confounding factor, that is a factor which would be a confounder if these two conditions were met in a data set of concern. Frequently, critics of epidemiological findings raise the possibility of confounding, citing numerous potential confounders, without attention as to whether these two conditions are, in fact, met.

Effect modification is distinct from confounding. It refers to circumstances in which the exposure/outcome relationship depends on the presence or absence (or level) of the modifying factor. In such circumstances, there are a series of risks for the outcome of interest associated with exposure, depending on level of the modifying factor.

The next two transparencies concern the theoretical example of particulate matter (PM), nitrogen dioxide (NO_2), and mortality. In many settings, PM and NO_2, have common sources and there is a potential for either confounding or effect modification. Of course, for NO_2 to be a confounder, it would need to be a predictor of mortality, an association that has not been consistently demonstrated. Thus, on the basis of understanding of toxicology of NO_2 and the epidemiological data available, it would not be a candidate to be a confounder.

In the diagram labeled "causal", I have indicated that particulate matter is associated with increased risk for mortality. NO_2 and PM concentrations may be associated because of their common sources, but the diagram does not link NO_2 with increased mortality, reflecting understanding of its toxicity.

Next on the page, the example is designated "causal pathway". In this example, NO_2 is in the causal pathway for the increased risk of mortality associated with PM. It contributes to the

formation of secondary particles, which are the actual toxic agents. NO^2 concentration (or its sources) might be considered as a "surrogate" for the proximal causal agent, PM.

The third transparency provides diagrams for confounding and modification. As already mentioned, NO_2 is an unlikely confounder, given the lack of evidence of the increase in mortality with rising NO_2 concentrations. However, assuming that it were a risk factor for increased mortality, the diagram represents the relationships for confounding. If NO_2 level modified the effect of PM, then a set of relative risks describing the association of PM with mortality would be derived, corresponding to the strata of NO_2.

There are a number of other epidemiological concepts to be considered in the Criteria Document:

- **Confounding versus potential confounding: Throughout the document there should be careful attention to whether conditions for confounding are met. As noted, raising the possibility of confounding does not mean that confounding is actually present.**

- **Interaction:** In places, the term "interaction" is used, generally in place of effect modification. Interaction properly refers to the statistical terms used in a model to assess effect modification.

- **The mixture problem:** Admittedly, ambient air pollution is a complex mixture, of which PM is one component. Nonetheless, the Clean Air Act has designated PM and other "criteria" pollutants for regulation. Study designs and data analysis are directed at attempting to characterize the effects of PM and these other pollutants, and not that of the mixture itself. The criteria pollutants provide some indication of the characteristics of these mixtures and consideration of effect modification represents an indirect approach to understanding the toxicity of mixtures. The Criteria Document should acknowledge the mixture issue and the related requirements of the Clean Air Act specifically.

- **Measurement Error:** This is a key issue that should be addressed in Chapters 5 and 6. Throughout the document, the concept of measurement error is considered but the underlining formulations are variable and not necessarily accurate. The document should be made uniform for this key issue. The consequences of measurement error are complex and its potential consequences should be listed, at least in a general fashion.

- **Heterogeneity :** The Criteria Document considers the heterogeneity of risk estimates across the United States. This heterogeneity cannot be completely explained by available, but crude, indicators. Heterogeneity does need to be explained, but its presence is not a barrier to interpreting the findings on particulate matter. Additionally, summary estimates at a national level can be made in the face of heterogeneity as they intrinsically weight the U.S. population's exposure by the underlying distributional modifying factors.

Interpretation of epidemiological data: Chapter 6 offers a relatively literal interpretation of the epidemiological evidence, absent a clear biological framework. In interpreting epidemiological data, the need for a foundation in biological understanding is evident. However, Chapter 6 as presently authored, makes little connection to the substantial literature that is reviewed in other chapters. These connections should be made in Chapter 6 and then reinforced in Chapter 9.

George Taylor, PhD

Air Quality Criteria for Particulate Matter: Chapter 4 (Environmental Effects)
General Comments

There are eight overarching comments on the issue of PM and ecological effects.

1. The consequences of particulate matter (PM) for welfare issues are largely relegated to visibility. The effects on vegetation and ecosystems of ambient levels of PM are regarded as being trivial and do not require substantive discussion. In contrast, the consequences of PM on human health are highly significant, well characterized and easily quantifiable in economic and human health dimensions. This (human health) is where the emphasis needs to be directed.

2. In light of the above, the CD is VERY excessive in its discussion of PM effects. The excessiveness can be traced to several issues. The first is inclusion of topics that simply are not relevant or are trivial. The second is the depth of discussion of issues that probably could be succinctly presented in 50% or less space. The third is the "handle" applied to the issue of sulfur and nitrogen inputs. This is a PM CD and sulfur and nitrogen are small contributors to the nitrogen and sulfur inputs to landscapes. The breadth and depth of attention to nitrogen and sulfur far exceeds the environmental concern as it is related to PM.

3. One of the major ecosystems affected by PM deposition and for which EPA has heavily invested in R&D is deposition of particles to surface waters. The most notable studies are ones from the Great Lakes and to a lesser degree the Chesapeake. It is important that these systems be included.

4. By length alone, one might conclude that the nitrogen or sulfur issue is driven by PM. This misinformation might be translated by policy makers into thinking that changes in PM will affect significantly such issues as nitrification, etc. Since most (>80%) of the nitrogen and sulfur that enters continental landscapes comes through processes other than PM, it is not appropriate to present the information as currently presented in the CD.

5. The human health chapters do a creditable job of linking the sections on atmospheric chemistry with the effects on human health. In the sense of a risk assessment, there is a tidy linkage between exposure and effects. This linkage is missing altogether in the section on environmental effects. There is no effort to relate the PM in the atmosphere to effects in terrestrial or aquatic landscapes. The consequence is that the chapter fails one of the basic premises of risk assessment. It is strongly recommended that the chapter better establish a linkage between exposure and effects. Or, the other option is to simply delete the nitrogen and sulfur topics from the PM CD.

In looking over the chapters on the atmospheric chemistry of PM, there is little quantitative discussion of the magnitude of sulfur and nitrogen in PM. Although both are discussed, it is difficult to see how the environmental chapter could be so "loaded" with nitrogen and sulfur when the atmospheric chapter does not heavily present the same information.

6. The final overarching issue is a derivative of the above. The conclusions portray the potential for PM to be a major stress on continental landscapes in the US. This is largely driven by the obsessive discussion of nitrogen and sulfur and by the failure to effectively link exposure in the atmosphere to effects. The conclusion is more alarmists than needs to be portrayed and the data simply do not reflect that degree of concern. More realism is needed in the assessment.

7. Deposition is missing from this CD. For ecosystems, there is a critical linkage between atmosphere concentration and effects and the vector is deposition. It is important to have a section devoted to deposition so there is a frame of reference for know what the inputs to

ecosystems are. There are a host of papers that address this issue and at least some should be cited.

8. In looking at PM per se, it is interesting to note that the chapter fails to mention to one type of ecosystem for which deposition of PM is likely to be very important – urban and suburban forests (largely in parks). There is a great deal of literature on these systems. In fact, it might be best to replace the current discussion of deposition to the IFS sites and replace that material with the urban suburban forest analysis.

Specific Issues

1. There is little reason to consider in much depth the consequences of PM on vegetation and ecosystems. In fact, most of the material in Chapter 4 characterizing the effects on vegetation and ecosystems could be reduced by 50% or more. Much of the information is appropriate to other documents (e.g., deposition of sulfur and nitrogen) but is only tangentially (at best) related to PM and the standard setting process.
2. The discussion of wet and dry deposition on ecosystem processes is largely a function of research conducted in the east where precipitation is the major mode of deposition. In the western US, dry processes are far more important as a vector for deposition. It is recommended that the research in the West be given some parity in the discussion assuming that the discussion of deposition remains. In light of No. 1 (above), this issue may be moot.
3. The discussion of direct effects of PM on vegetation (4.2.1) is appropriate to this document but has no relevance to the standard setting process since effects are seen at levels well above ambient rates of deposition. This section could be reduced in length by 75% or more.
4. The discussion of the consequences of nitrogen input to ecosystems (4.2.1.2) is hard to justify in the depth presented. If it is important to include, it is recommended that the dissimilarity between the eastern and western US be highlighted.
5. The same concern for sulfur is appropriate. The detail is only tangentially related to the issue of PM and the deposition is unlikely to be of consequence.
6. On page 4-22, reference is made to the fact that ecosystem level responses to stress begin at the population level. I am not quite sure that is accurate.
7. On page 4-24, the following statement is offered, "In contrast, anthropogenic stresses usually are severe, debilitating stresses". I find it difficult to agree with this statement. In the same paragraph, the four categories of stresses seem to be awkward. Where would nitrogen deposition or CO2 increase fall in this scheme?
8. On page 4-25, reference is made to the concept of secondary succession and chronic stresses. The concept of secondary succession as presented is not accurate and the syntax of those sentences is not accurate. The entire process of secondary succession is a dated concept in ecology and its relevance here is marginal.
9. On page 4-26, the comment is made that it is difficult to determine responses of ecosystems to stress. As a blanket statement, this is simply not accurate. Maybe the magnitude of the response is not known with certainty but the direction and many of the changes are known with certainty.
10. The section on particulate matter, atmospheric turbidity and effects on vegetation processes (page 4-34) is weak from a cause-effect perspective. This could be deleted.
11. Is the section on solar UV radiation (p4-39) needed in this document? The argument is tenuous.
12. The conclusion paragraph (4-84) is too bold a statement regarding the effects. The lead should be less alarmist and simply state that there is little reason to address secondary effects of PM on vegetation and ecosystem processes. It is important to be accurate, particularly in the summary sections.
13. On pages 4-113, the work of Chestnut and Davis is presented on the willingness to pay for visibility. It is important that the results and conclusions of the authors be reported rather than simply that they conducted a study.
14. If one is discussing nitrogen and sulfur in the PM document, then all of the other

atmospheric stressors associated with PM should be included as well. These would include base cations, hydrogen ions, heavy metals, pesticide residues, oxidants, etc. An alternative would be to simply list these as part of the deposition process but not relevant to the CD.

15. The processes discussed governing how PM affects vegetation are only a fragment of the physics, chemistry and biology of PM. The concepts to be included should be effects of velocity and particle size on deposition, solubilization, evapoconcentration, rainfall events, wash off, re-suspension, transcuticular migration, etc.
16. Deposition to surface waters is entirely missing in the CD and yet this is a major issue for understanding estuaries and lakes. There is a host of data for this topic for major resources and the largest set of data is for the Great Lakes. Its omission in light of what is included (e.g., nitrogen and sulfur at IFS sites) is a problem

Ronald H. White, M.S.T.

Chapter 6: Epidemiology of Human Health Effects from Ambient Particulate Matter - General Comments

Overall, this chapter presents a comprehensive review of the extensive body of epidemiological studies published since completion of the 1996 particulate matter criteria document. The chapter properly interprets the studies discussed and appropriately emphasizes the strengths and weaknesses of the current scientific evidence of the health effects of particulate matter.

One key issue that requires further attention is the need for a consistent approach with explicit criteria throughout the chapter for the selection of the analyses from the studies included for summarization in the tables. For example, there are several criteria described (pg. 184; lines 8 –17) as providing the basis for selection of the analyses summarized in Table 6-19 and 6-20. However other summary tables do not explicitly provide the criteria for the selection of analyses summarized in the tables. Providing these criteria make the approaches used in selecting the analyses included for summarization in these tables and avoid concerns regarding author bias in the selection of analyses included for summarization.

The discussion of the infant mortality/related morbidity studies that have been published since 1996 should be expanded. These data are important new findings that significantly augment the more limited data available in the 1996 CD. A table summarizing these studies should also be included in the chapter.

The discussion of lung cancer associated with PM exposure in the long-term prospective studies should be expanded and receive additional attention in the text. Given the finding of a statistically significant association of PM and lung cancer in the recent expanded ACS study analysis by Pope, which I would presume will be included in the next revision of the CD, this health endpoint deserves substantial further elaboration and emphasis. In addition, the entire diesel particulate health effects literature regarding lung cancer is not referred to in this discussion. Recognizing that the EPA Diesel Particulate Health Assessment document reviews this literature in detail, the relevant science should be summarized in this chapter's discussion of the lung cancer issue and the reader referred to the Diesel Health Assessment document for a more complete discussion of this scientific literature.

Specific Comments

Pg. 6-226: This discussion regarding alternative methodological approaches to addressing confounding omits reference to the selection of study areas where potentially confounding air pollutant levels are relatively low (e.g. Vedal's 1998 study of asthmatic and nonasthmatic children in Port Albeni, B.C.).

Appendix 6A and 6B: There is no explanation in Chapter 6 as to the rationale for the inclusion of

these appendices. While the recent studies regarding the relationship of heart rate variability to PM exposure provides one possible biological mechanism for the cardiac effects that may cause morbidity and ultimately premature mortality, other potential mechanisms for cardiovascular effects have also been identified (e.g. plasma viscosity, coagulation). The NMAPS data in Appendix 6B should be integrated into the body of Chapter 6, with the daily deaths expressed as an age adjusted rate as well as number of deaths.

Pg. 6-138: The use of the term "recent" in reference to the 1997 study by Peters et. al. is inappropriate in a document that will be released in 2002. The use of this adjective with respect to studies in this entire chapter should be reviewed to ensure that only studies published in the last year or so are referred to as "recent", or alternatively the adjective should be eliminated from the chapter's discussion of studies.

Chapter 9: Integrated Synthesis: Particluate Matter Atmospheric Science, Air Quality, Human Exposure, Dosimetry, and Health Risks - General Comments

While this chapter is somewhat improved compared to the previous draft in terms of writing style and providing some integration of information from different scientific disciplines, the underlying flawed approach of providing sequential summaries of what has already been summarized in previous chapters is retained. As such, this crucial chapter still does not provide the reader with a true integration of the key information identified in the previous chapters as being of major significance for the air quality standard-setting process.

In my December 1999 comments on the previous draft of this chapter, I had suggested an approach that would structure the information provided in this chapter as responses to several key questions regarding the health science information published since the previous Criteria Document. In his written comments on this current chapter, Dr. David Bates has also suggested a somewhat similar approach to structuring this chapter. As it currently is written, there is a significant amount of repetition of information already provided and summarized in the previous chapters. Key new information regarding PM exposure, toxicology, clinical studies and epidemiology are not currently integrated in a manner that informs the standard-setting process.

Specific Comments

Pg. 9-65; lines 2-5: The data audit performed for the HEI Reanalysis Project was not conducted by the study investigators as currently indicated in the text. The data audit was performed by an independent team selected by HEI to perform this function for the study.

Warren White, PhD

4.3 Effects on Visibility - First impressions

The visibility portions of the March 2001 draft CD were prematurely circulated for external review. Their inferiority relative to other parts of the document underscores the Agency's long-standing disdain for this subject. I can think of no harsher criticism of the material than simply reproducing a few of the highlights. Keep in mind that all come from fewer than two dozen pages!

Some of the lines could have been written by Edward Lear:

"Light absorption by aggravated carbon at visible wavelengths is enhanced by no more than 30% and diminishes if encapsulated by a nonabsorbing aerosol." (P4-90, L 19)

"At the surface, a variable fraction of the solar radiation is reflected back upwards, referred to as surface reflectance or the albedo, illuminating the atmosphere from above and below." (P 4-88, L 4)

"The increase was largest in the summer and decreased in the winter." (P 4-108, L 28)

"Some of the visibility impairment in northern California and Nevada, including Oregon, southern Idaho and western Wyoming, ..." (P 4-109, L 16)

"Horvath (1993) reported that measured light absorption efficiencies for light absorbing carbon ranges from 3.8 to 17 m^2/g. According to Horvath (1993), calculated absorption efficiencies are too high, ranging from 8 to 12 m^2/g for monodispersed carbon particles." (P 4-90, L 12)

"For most rural eastern sites, sulfates accounts for >60% of the annual average light extinction on the best days .." (P4-108, L 23)

"However, several sites are not showing steady improvements in either visibility or $PM_{2.5}$, particularly in the number of worst visibility days (90^{th} percentile)." (P 4-111, L 20) [In other words, the number of days in a year is holding steady at about 365 per.]

There are tautologies and circular definitions of the sort associated with Lewis Carroll:

"Human vision is one of the factors that affects the way an object is viewed." (P 4-86, L 10)

"Discoloration may be used as a quantitative measurement of atmospheric color changes in urban hazes." (P 4-98, L 2) [In much the same way as morbidity can be used as an indicator of impaired health.]

"The light-extinction coefficient is the quantitative measure of haziness, defined as σ_{ext} = K/visual range, where K is the Koschmieder constant. The value of K is determined both by the threshold sensitivity of the human eye and the initial contrast of the visible object against the horizon sky. The visual range may be calculated from the light-extinction coefficient using the Koschmieder equation .." (P 4-94, L 23)

There is simple technical ignorance:

"The cones, a receptor cell in the retina, govern visibility interpretations." (P 4-86, L12) [This is why an eyeball can be offended by haze even after surgical removal from the head. And why we see nothing after sundown.]

"Some of the light in the sight path is absorbed or scattered towards the observer. The remaining light is absorbed or scattered in other directions." (P4-86, L 24) [Leaving the observer searching in vain for any transmitted image.]

"The scattering and absorption efficiencies are determined by estimating the size distribution of each particle." (P 4-89, L 20)

".. the extinction coefficient that is calculated from the visual range, corrected to 60% relative humidity by the Koschmeider relationship." (P 4-109, L 29) [Versatile guy, that K.]

"Mie scattering is the scattering of all visible wavelengths equally (Shodor Education Foundation, Inc., 1996)." (P 4-87, L 1) [Which must be why Mie theory is computationally so trivial. Distressingly, this claim is supported by the citation, which turns out to be on-line training material developed for the Agency. The cited page also explains "how the shorter wavelengths which our eyes detect as blue when mixed, are scattered at a right angle. If the sun

is directly overhead, the sun and sky look almost white while the sky is blue off to the sides in the direction of the scattered light." The student might wish to step outside some clear day and check whether the horizon is indeed blue and the sky white.]

"The output of the Mie calculations includes efficiency factors for extinction, Q_{ext}, scattering, Q_{scat}, and absorption, Q_{abs}. The Q_{ext}, Q_{scat}, and Q_{abs} give the fraction of the incident radiation falling on a circle with the same diameter as the particle that is either scattered or absorbed. The light scattering or absorption efficiency factor (in units of m^2/g) is the change in the light scattering or absorption efficiencies per unit change in mass of the fine particle constituent. ... Multiplying the values of the light scattering efficiency factor by the aerosol volume concentration (in units of $\mu m^3/cm^3$) gives the value of the light-scattering coefficient, σ_{sp}, (in units of Mm^{-1}) for these particles." (P 4-89, L 15-26) [Students: find 3 different concepts of 'efficiency factor' in this paragraph. For extra credit, find 4 or more.]

".. over a 30-year period (1940 to 1990)." (P4-111, L 3)

There are misstatements of the Agency's own key regulatory concepts:

"Visibility impairment is defined as any humanly perceptible change in visibility (light extinction, visual range, contrast, or coloration)." (P 4-85, L 3) [The hypothetical observer in a pure Rayleigh atmosphere thus experiences impaired visibility during each sunset and sunrise. Will the Sierra Club have to sue before the Agency addresses the long-standing and pervasive problem of twice-daily twilight?]

"$dv = 10\ log_{10}\ (s_{ext}\ /10\ Mm^{-1})$" (P 4-95, L 13) [This makes one deciview correspond to a 26% rather than 10% change in extinction, and makes an extinction coefficient of 100 Mm^{-1} correspond to 10 dv rather than the 23 dv indicated in Figure 4-20. To be fair, this error is accurately reproduced from the 1996 CD, and is faithfully carried into the 2001 Staff Paper.]

Currency, competence, and relevance, by subsection

What are appropriate standards for review? In terms of currency and competence, a default option for the 2001 CD is to reprint the 6+ page summary of visibility effects from the 1996 CD, section 8.9.1. That text is clear and accurate. If new text is needed, it should be no less clear and accurate. In terms of relevance, I start from the presumption that any secondary standard for PM will be specified in terms of the health-based primary standard, currently $PM_{2.5}$ as defined by the FRM. A key burden of section 4.3, then, is to document a consistent relationship between visibility and measured fine particle mass.

4.3.1 **Introduction:** The second of the two paragraphs is up to date and appropriate (although the citation of the IWAQM document (USEPA 1995a) is puzzling). The first paragraph, in contrast, is confused and unnecessary – why should the 2001 CD open its visibility update with a garbled rehash of the Agency's 1979 distinction between reasonably attributable and regional haze?

4.3.2 **Factors affecting atmospheric visibility:** There is nothing in here drawn from work done since 1996, save for a passing reference to current visibility conditions from the Agency's latest trend report. Instead, there are odd definitions (e.g. "The visual range is the closest distance ..."), unused definitions (e.g. multiple scattering), incorrect definitions that were treated correctly in the 1996 CD (e.g. Mie scattering, as already noted), and a similarly varied range of 'facts'. It is dispiriting to find the Agency discarding a document that this Committee spent two years reviewing, in order to slap together an erratic new assemblage that is no more up-to-date.

Is visibility (as crudely indexed by, say, visual range) inversely related to ambient particle concentration (as crudely indexed by, say, $PM_{2.5}$)? One surely couldn't establish

that point from this review! "Visibility impairment *may be* connected to air pollutant properties... Human vision is one of the factors ... the appearance of a distant object is determined by illumination of the sight path ... Visibility within a sight path longer than approximately 100 km .. is affected by changes in the properties of the atmosphere over the length of the sight path."

4.3.3 **Optical properties of particles:** Of the 23 different papers cited in this subsection, 17 were published by 1994 and 13 were reviewed in the 1996 CD. The technical discussion is very confused, and diverse extinction efficiencies are jumbled together with no context.

The Staff Paper includes a cross-plot (Figure 5-2) of ASOS airport visibility data versus 24-h $PM_{2.5}$ concentrations at Fresno, CA. This is exactly the sort of analysis that is needed to support a $PM_{2.5}$ standard for visibility and is missing from the CD. But it is only the first step: is the rest of the country just like Fresno? The CD instead gives us indigestible factoids: "Richards et al. (1991) reported a scattering efficiency for fine particles of ammonium sulfate of 1.2 m^2/g .. Sulfate scattering efficiencies have been reported to increase by a factor of two when the size distribution went from 0.15 to 0.5 µm .. The calculated scattering efficiencies for sulfates were 4.1 m^2/g for 100% mass removal and 3.4 and 5.6 m^2/g for 25% mass removal. Calculated scattering efficiencies for carbon particles ranged from 0.9 to 8.1 m^2/g .."

4.3.4 **Effect of relative humidity:** This section cites a higher proportion of recent work and is better written.

4.3.5 **Measures of visibility:** Of the 24 different papers cited in this subsection, 17 were published by 1994 and 13 were reviewed in the 1996 CD. I don't see any new information.

And including "fine particulate matter concentrations" as a "measure of visibility" is rather begging the whole question, is it not? The figure (4-22) supporting this subsection simply *assumes* a relationship for which the previous subsections laid no theoretical or empirical basis. (Note that the assumed Koschmieder coefficient in this figure differs from that used in the next (4-23).)

4.3.6 **Visibility monitoring methods and networks:** The new ASOS and expanded IMPROVE networks are appropriate topics for inclusion in this CD. The extinction budgets in Table 4-7 are problematic, however, because the text has given no theoretical or empirical basis for constructing and understanding them. It would better support a visibility-based secondary standard to summarize the measured extinction/$PM_{2.5}$ ratios and regression relationships observed at those sites with optical data.

4.3.7 **Visibility modeling:** Modeling can't be credible until the science is, so I didn't bother with this subsection.

4.3.8 **Trends in visibility impairment:** Much of this subsection (P 4-109, L 4-26) concerns extinction budgeting rather than trends in space and time. As noted above at subsection 4.3.6, the text has laid no basis for such apportionment. Moreover, some of the characterizations are a bit suspect -- for example, the statement "In several areas of the west, sulfates account for over 50% of the annual average aerosol extinction" is not supported by Table 4-7.

The trend discussion is largely carried over from the 1996 CD; Figure 4-23 is an update of Figure 6-112 by only three years and Figure 4-24 is a reprint of Figure 6-113. Considering that this is supposed to be an incremental update of the 1996 CD, and that

the data in Figure 4-24 end in 1992, it is hard to justify open-ended statements like "The haziness over the Gulf states increased between 1960 and 1970 and remained virtually unchanged since then."

4.3.9 **Economics of PM visibility effects:** Here, finally, is a subsection that does not just rehash and garble the corresponding 1996 account. Unfortunately, the new account seems inconsistent with the old, and the disagreement is nowhere acknowledged. According to the 2001 review (P 4-114, L 2), "The results indicate a willingness to pay per deciview improvement in visibility [in class I areas, capturing both use and nonuse recreational values] of between $5 and $17 per household." According to the 1996 review (Table 8-6), the willingness to pay per deciview improvement in urban visibility ranged from $8 to $231 per household (in older, more valuable dollars), with a median of about $100. If visibility is really worth that much more in cities than in National Parks, then why are almost all our visibility monitors in Parks? I couldn't find the $5 - $17 values in the cited reference, so I suspect that this is yet another instance of garbled reporting.

The bottom line for section 4.3 is that no coherent attempt is made to connect visibility with the health-based PM indicator.

A curious omission

The single most important visibility development since the 1996 CD has been the arrival of Regional Haze Rules. These Rules establish a framework for regulating visibility that any secondary PM standard will have to coexist with. Whereas any secondary standard will require scientific review by CASAC, the Regional Haze Rules already in effect were developed largely from an administrative/bookkeeping perspective. How does the Regional Haze bookkeeping square with the science reviewed by the CD? This is a question the draft studiously ignores.

George T. Wolff, PhD

Chapter 1

1. p 1-8, lines 4 – 5 – Is this something new? CASAC has not had an opportunity to comment collectively on the proposals in the past.

2. p 1-14, lines 1 – 2 – Does this mean that higher concentration studies that show no effect were ignored?

Chapter 2

General – The chapter needs a glossary.

1. p 2-15, lines 2-6 – This appears to be worded too strongly given the conclusions reached in chapter 6 (see page 6-266, lines 29-30).

2. p 2-18, line 23 – The photolysis of O_3 is the major source of OH only in relatively pristine atmospheres. The major source in urban atmospheres is likely organic gases.

3. P 2-19, lines 1-5 – This is also too strongly worded for the same reasons as 1.

4. P 2-20, lines 1-3 – While this statement is true for sulfates, it is not for nitrates. Because of thermal decomposition at high ambient temperatures, nitrates particles tend to be higher in the winter.

5. P 2-33, line 16 – I would remove the word "significantly" since droplet acidity is dominated by in cloud formation and acid gas scavenging. Same comment for p 2-101, line 15.

6. P 2-86, section 2.2.5.1 – A short description of the TEOM is needed.

7. Section 2.2.5 – Except for the TEOM, it is not clear if all of the devices mentioned in this section are Class III FRMs.

8. Section 2.2.6 – "Data quality" section – Can anything be said about the magnitude of the measurement error that would shed some light on the exposure errors associated with the various epidemiology studies? It is mentioned that the coarse numbers are "inherently less precise." Can that be quantified and put in perspective given that the epi studies have a tendency to attribute a lower risk associated with the coarse mass relative to the fine and PM10 mass?

9. p 2-104 lines 3-4 – The is something wrong with the sentence that begins "Fresh, submicron-size…."

Chapter 3

1. p 3-10, lines 4-8 – This should be expanded to include more quantitative information on the trends of specific constituents.

2. p 3-12, line 10 – Define FRM.

3. P 3-13, figure 3-7a – This figure needs more reference ticks on the y-axis and a better legend explaining the meanings of the various symbols. What is the center bar and what is +?

4. P 3-16, figure 3-8 – Something is needed to distinguish between the PM2.5 and PM10 bars.

5. P 3-35, table 3-7, organic carbon row, anthropogenic column – delete "emitted by motor vehicles" since there are other man-made sources of hydrocarbons.

Chapter 6

1. General Comment – When discussing the inclusion of gaseous pollutants in any analysis, it is insufficient to merely say pollutant x was included without specifying which measure of the pollutant was used. This is particularly important for O_3. In time series studies, the 1-hr or 8hr max are the appropriate measures to use not the 24-hr average which will introduce unnecessary measurement error into the analysis and mask the true effect. In the cross-sectional studies, the mean of the 1-hr daily max is the appropriate measure, not the annual mean. The measure should be clearly indicated for each study, so the reader can make judgements about the validity of the results. The same comments apply to meteorological measurements.

2. General Comments – Some consistent rules need to be established about identifying the level of statistical significance of results and their inclusion in subsequent discussions. As it stands now, it appears that results are included regardless of significance level if they support a desired conclusion.

3. P 6-1, lines 8-11 – Change "measurable excesses" to "statistical associations between," and "being associated with" to "and."

4. Table 6-1 – The specific measure of the gaseous co-pollutants and meteorological variables should be included in this and other summary tables.

5. Comments on the measures used in NMMAPS and the HEI Reanalysis Study – Since these 2 studies are highlighted in the CD to illustrate a number of points including the small or nonexistent effect of ozone on the PM signal, a few comments on these studies are in order. NMMAPS used the 24-hour average concentrations for gaseous pollutants including O_3 and CO. This averaging time, while consistent with the averaging time of PM, whose relevant

health-response time at ambient levels remains unknown, has two major problems. First, it is inconsistent with the known health-response times of both O_3 and CO. As a result, the impacts of O_3 and CO on the regression are not properly characterized. Second, the 24-hour averages of O_3 and CO do not correlate perfectly with the peak 1-hour or 8-hour values that are the measures associated with their health effect endpoints. Worse yet, urban sites tend to have higher peak O_3 than rural sites, but rural sites tend to have higher 24-hour O_3 concentrations than urban sites. For the spatial analysis, NMMAPS used annual means when it was appropriate to use the means of the 1-hour or 8-hour daily maxima. Cleaner areas and rural areas generally have higher annual average ozone values than more polluted urban areas. Consequently, the results involving O_3 and CO are likely not meaningful.

6. The Reanalysis Team also used the same annual average O_3 for the H6CS reanalysis. Although the report states that they used the annual mean of the daily 1-hour maxima for the ACS reanalysis, they used the annual average as well because the ozone values presented in appendix G of the report are much too low to be the average of the 1-hour maxima. Another problem with computing a valid annual mean for ozone is that many locations only measure ozone during the ozone season, which has a different definition depending upon the local climatology. In Michigan, which is typical of northern states, ozone is only measured from April 1 to September 31, whereas in Southern California, it is measured year round. Consequently, I have the same similar concerns for the Reanalysis multi-pollutant results as I have for the NMMAPS results.

Chapter 9

1. P 9-2, line 30 – Delete "in general."

2. Table 9-2, organic carbon row, anthropogenic column – delete "emitted by motor vehicles" since there are other man-made sources of hydrocarbons.