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

February 16, 2006

EPA-CASAC-CON-06-003

**OFFICE OF THE ADMINISTRATOR**
**SCIENCE ADVISORY BOARD**

Honorable Stephen L. Johnson
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Clean Air Scientific Advisory Committee (CASAC) Ozone Review Panel's Consultation on EPA's First Draft Ozone Staff Paper, Risk Assessment, and Exposure Assessment Documents

Dear Administrator Johnson:

EPA's Clean Air Scientific Advisory Committee (CASAC), supplemented by subject-matter-expert Panelists — collectively referred to as the CASAC Ozone Review Panel ("Panel") — met in a public meeting held in Durham, NC, on December 8, 2005, to conduct a consultation with staff from EPA's Office of Air Quality Planning and Standards (OAQPS), within the Office of Air and Radiation (OAR), on EPA's *Review of the National Ambient Air Quality Standards for Ozone: Policy Assessment of Scientific and Technical Information* (first draft Ozone Staff Paper, November 2005); and two related draft technical support documents, *Ozone Health Risk Assessment for Selected Urban Areas: First Draft Report* (first draft Ozone Risk Assessment, November 2005) and *Ozone Population Exposure Analysis for Selected Urban Areas: Draft Report* (first draft Ozone Exposure Assessment, October 2005).

The SAB Staff Office has developed the consultation as a mechanism to advise EPA on technical issues that should be considered in the development of regulations, guidelines, or technical guidance before the Agency has taken a position. A consultation is conducted under the normal requirements of the Federal Advisory Committee Act (FACA), as amended (5 U.S.C., App.), which include advance notice of the public meeting in the *Federal Register*.

As is our customary practice, there will be no consensus report from the CASAC as a result of this consultation, nor does the Committee expect any formal response from the Agency. The current CASAC roster is attached as Appendix A of this letter, and the CASAC Ozone Review Panel roster is found in Appendix B. EPA's charge to the Panel is contained in Appendix C to this letter, and Panelists' individual written comments are provided in Appendix D.

Sincerely,

***/Signed/***

Dr. Rogene Henderson, Chair
Clean Air Scientific Advisory Committee

Appendix A – Roster of the Clean Air Scientific Advisory Committee

Appendix B – Roster of the CASAC Ozone Matter Review Panel

Appendix C – Charge to the CASAC Ozone Review Panel

Appendix D – Comments from Individual CASAC Ozone Review Panelists

# Appendix A – Roster of the Clean Air Scientific Advisory Committee

## U.S. Environmental Protection Agency
## Science Advisory Board (SAB) Staff Office
## Clean Air Scientific Advisory Committee (CASAC)

### CHAIR

**Dr. Rogene Henderson**, Scientist Emeritus, Lovelace Respiratory Research Institute, Albuquerque, NM

### MEMBERS

**Dr. Ellis Cowling**, University Distinguished Professor-at-Large, North Carolina State University, Colleges of Natural Resources and Agriculture and Life Sciences, North Carolina State University, Raleigh, NC

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

**Dr. Philip Hopke**, Bayard D. Clarkson Distinguished Professor, Department of Chemical Engineering, Clarkson University, Potsdam, NY

**Dr. Frederick J. Miller**, Consultant, Cary, NC

**Mr. Richard L. Poirot**, Environmental Analyst, Air Pollution Control Division, Department of Environmental Conservation, Vermont Agency of Natural Resources, Waterbury, VT

**Dr. Frank Speizer**, Edward Kass Professor of Medicine, Channing Laboratory, Harvard Medical School, Boston, MA

**Dr. Barbara Zielinska**, Research Professor, Division of Atmospheric Science, Desert Research Institute, Reno, NV

### SCIENCE ADVISORY BOARD STAFF

**Mr. Fred Butterfield**, CASAC Designated Federal Officer, 1200 Pennsylvania Avenue, N.W., Washington, DC, 20460, Phone: 202-343-9994, Fax: 202-233-0643 (butterfield.fred@epa.gov) (Physical/Courier/FedEx Address: Fred A. Butterfield, III, EPA Science Advisory Board Staff Office (Mail Code 1400F), Woodies Building, 1025 F Street, N.W., Room 3604, Washington, DC 20004, Telephone: 202-343-9994)

# Appendix B – Roster of the CASAC Ozone Review Panel

## U.S. Environmental Protection Agency
## Science Advisory Board (SAB) Staff Office
## Clean Air Scientific Advisory Committee (CASAC)
## CASAC Ozone Review Panel

**CHAIR**

**Dr. Rogene Henderson***, Scientist Emeritus, Lovelace Respiratory Research Institute, Albuquerque, NM

**MEMBERS**

**Dr. John Balmes**, Professor, Department of Medicine, University of California San Francisco, University of California – San Francisco, San Francisco, California

**Dr. Ellis Cowling***, University Distinguished Professor-at-Large, North Carolina State University, Colleges of Natural Resources and Agriculture and Life Sciences, North Carolina State University, Raleigh, NC

**Dr. James D. Crapo***, Professor, Department of Medicine, Biomedical Research and Patient Care, National Jewish Medical and Research Center, Denver, CO

**Dr. William (Jim) Gauderman**, Associate Professor, Preventive Medicine, Medicine, University of Southern California, Los Angeles, CA

**Dr. Henry Gong**, Professor of Medicine and Preventive Medicine, Medicine and Preventive Medicine, Keck School of Medicine, University of Southern California, Downey, CA

**Dr. Paul J. Hanson**, Senior Research and Development Scientist, Environmental Sciences Division, Oak Ridge National Laboratory (ORNL), Oak Ridge, TN

**Dr. Jack Harkema**, Professor, Department of Pathobiology, College of Veterinary Medicine, Michigan State University, East Lansing, MI

**Dr. Philip Hopke**, Bayard D. Clarkson Distinguished Professor, Department of Chemical Engineering, Clarkson University, Potsdam, NY

**Dr. Michael T. Kleinman**, Professor, Department of Community & Environmental Medicine, University of California – Irvine, Irvine, CA

**Dr. Allan Legge**, President, Biosphere Solutions, Calgary, Alberta, Canada

**Dr. Morton Lippmann**, Professor, Nelson Institute of Environmental Medicine, New York University School of Medicine, Tuxedo, NY

**Dr. Frederick J. Miller***, Consultant, Cary, NC

**Dr. Maria Morandi**, Assistant Professor of Environmental Science & Occupational Health, Department of Environmental Sciences, School of Public Health, University of Texas – Houston Health Science Center, Houston, TX

**Dr. Charles Plopper**, Professor, Department of Anatomy, Physiology and Cell Biology, School of Veterinary Medicine, University of California – Davis, Davis, California

**Mr. Richard L. Poirot***, Environmental Analyst, Air Pollution Control Division, Department of Environmental Conservation, Vermont Agency of Natural Resources, Waterbury, VT

**Dr. Armistead (Ted) Russell**, Georgia Power Distinguished Professor of Environmental Engineering, Environmental Engineering Group, School of Civil and Environmental Engineering, Georgia Institute of Technology, Atlanta, GA

**Dr. Elizabeth A. (Lianne) Sheppard**, Research Associate Professor, Biostatistics and Environmental & Occupational Health Sciences, Public Health and Community Medicine, University of Washington, Seattle, WA

**Dr. Frank Speizer***, Edward Kass Professor of Medicine, Channing Laboratory, Harvard Medical School, Boston, MA

**Dr. James Ultman**, Professor, Chemical Engineering, Bioengineering Program, Pennsylvania State University, University Park, PA

**Dr. Sverre Vedal**, Professor, Department of Environmental and Occupational Health Sciences, School of Public Health and Community Medicine, University of Washington, Seattle, WA

**Dr. James (Jim) Zidek**, Professor, Statistics, Science, University of British Columbia, Vancouver, BC, Canada

**Dr. Barbara Zielinska***, Research Professor, Division of Atmospheric Science, Desert Research Institute, Reno, NV

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* Members of the statutory Clean Air Scientific Advisory Committee (CASAC) appointed by the EPA Administrator

# Appendix C – Charge to the CASAC Ozone Review Panel

Within each of the main sections of the first draft Staff Paper, questions that EPA's Office of Air Quality Planning and Standards (OAQPS) asks the Panel to focus on in their review include the following:

$O_3$ air quality information and analyses (Chapter 2):

1. To what extent are the air quality characterizations and analyses clearly communicated, appropriately characterized, and relevant to the review of the primary and secondary $O_3$ NAAQS?

2. To what extent are the properties of ambient $O_3$ appropriately characterized, including policy-relevant background, spatial and temporal patterns, and relationships between ambient $O_3$ and human exposure?

3. Does the information in Chapter 2 provide a sufficient air quality-related basis for the human health and environmental effects and assessments presented in later chapters?

$O_3$-related health effects (Chapter 3):

1. To what extent is the presentation of evidence assessed in the $O_3$ CD from the animal toxicology and controlled-exposure human experimental studies and epidemiologic studies, as well as the integration of information from across the various health-related research areas, technically sound, appropriately balanced, and clearly communicated?

2. What are the views of the Panel on the appropriateness of staff's discussion and conclusions on key issues related to quantitative interpretation of the epidemiologic study results, including, for example, exposure error, the influence of alternative model specification, potential confounding by co-pollutants, and lag structure?

3. What are the views of the Panel on the adequacy and clarity of staff discussions on the issue of potential thresholds in concentration-response relationships?

4. What are the views of the Panel on the appropriateness of the staff's characterization of groups likely to be sensitive to $O_3$?

Exposure Analysis (Chapter 4 of the draft $O_3$ Staff Paper and draft Exposure Analysis technical support document):

1. To what extent is the assessment, interpretation, and presentation of the initial results of the exposure analysis in Chapter 4 technically sound, appropriately balanced, and clearly communicated?

2. Are the methods used to conduct the exposure analysis technically sound? Does the Panel have any comments on the methods used?

3. Are the exposure analysis methods and results fully and clearly communicated in the draft Exposure Analysis technical support?

4. To what extent are the uncertainties associated with the exposure analysis clearly and appropriately characterized in both Chapter 4 and the draft Exposure Analysis technical support document?

5. What are the views of the Panel on sensitivity analyses that should be conducted to evaluate the influence of uncertainties in the exposure analysis?

Health Risk Assessment (Chapter 5 of the draft $O_3$ Staff Paper and draft Health Risk Assessment technical support document):

1. To what extent is the assessment, interpretation, and presentation of the initial results of the health risk assessment in Chapter 5 technically sound, appropriately balanced, and clearly communicated?

2. In general, is the set of health endpoints and concentration-response and exposure response functions used in the risk assessment appropriate for this review?

3. Are the methods used to conduct the health risk assessment technically sound? Does the Panel have any comments on the methods used?

4. Are the methods and results fully and clearly communicated in the draft Health Risk Assessment technical support document?

5. To what extent are the uncertainties associated with the health risk assessment clearly and appropriately characterized in both Chapter 5 and the draft Health Risk Assessment technical support documents?

6. What are the views of the Panel on sensitivity analyses that should be conducted to evaluate the influence of uncertainties in the health risk assessment?

Staff Conclusions and Recommendations on Primary $O_3$ NAAQS (Chapter 6):

1. What are the views of the Panel on the alternative primary standards identified by staff to be included in additional human exposure analyses and health risk assessments for the next draft $O_3$ Staff Paper?

$O_3$-related welfare effects (Chapter 7):

1. To what extent is the presentation of evidence drawn from the $O_3$ CD related to the various welfare effects considered in this review technically sound, appropriately organized and balanced, and clearly communicated?

2. To what extent does this first draft Chapter 7 appropriately take into account the range of views of the Panel members that were expressed orally and in writing during and after the consultation on the Environmental Assessment Plan?

3. To what extent do the figures aid in clarifying the text? Should more or less information of this type be included in the second draft?

4. To what extent does this draft recognize important sources of uncertainty associated with the various component analyses?

5. While recognizing the lack of quantitative information on $O_3$-related ecosystem effects, what are the Panel's views on the appropriateness of how this topic is addressed in this draft?

# Appendix D – Comments from Individual CASAC Ozone Review Panelists

This appendix contains the preliminary and/or final written comments of the individual members of the Clean Air Scientific Advisory Committee (CASAC) Ozone Review Panel who submitted such comments electronically. The comments are included here to provide both a full perspective and a range of individual views expressed by Panel members during the consultation process. These comments do not represent the views of the CASAC Ozone Review Panel, the CASAC, the EPA Science Advisory Board, or the EPA itself. Panelists providing written comments are listed on the next page, and their individual comments follow.

**Panelist** **Page #**

# Dr. Ellis Cowling

Dr. Ellis Cowling
North Carolina State University
December 17, 2005

## General Comments on the First Draft OAQPS Staff Paper on Ozone and Related Photochemical Oxidants: Policy Assessment of Scientific and Technical Information

### 1) Title of the Staff Paper

I agree with Philip Hopke's assertion that the title of the Staff Paper should be changed so it is faithful to the title of the National Ambient Air Quality Standards to which it applies. Since the Standards dealt with in this Staff Paper bears the name "Ozone and Related Photochemical Oxidants," the title of the staff paper should also include "Ozone and Related Photochemical Oxidants."

Maybe I missed it in the staff paper, but a clear listing of the various compounds covered by the phrase " and Related Photochemical Oxidants" would be beneficial. This is especially important since the photochemical processes leading to formation and accumulation of ozone, PAN and its homologues, formaldehyde, acetaldehyde, and other photochemical reaction products, are also involved in other air pollution problems. These other photochemical problems include formation and accumulation of:

a) secondary organic aerosols,

b) acidic and acidifying substances that contribute to the acidification of soils, surface waters, ground waters, and both aquatic and terrestrial ecosystems,

c) formation and oxidative modification of air toxics and their various reaction products,

d) depletion of stratospheric ozone, and

e) global climate change.

### 2) Introduction to the Staff Paper (Chapter 1)

It is very good that the general Introduction to the Staff Paper includes:

a) Concise summaries of both the legislative and litigation histories of these standards.

b) Careful definitions of the critically important terms "*indicator*, *averaging times*, *forms*, and *levels*" that are very important in understanding both primary and secondary standards.

c) Summaries of the several significant changes that have taken place in these primary and secondary standards for ozone and related photochemical oxidants since 1971.

d) References to each of the staff papers and criteria or other documents on ozone and related photochemical oxidants (1971, 1979, 1986, 1992, 1993, 1996, and 1997) that

preceded the 2005 2nd draft Criteria Document and the 2005 1st draft of the Staff Paper on ozone.

e) Direct quotations from the Clean Air Act describing how Congress directed the Administrator of EPA to use his or her professional judgment to identify air pollutants that "in his judgment, may reasonably be anticipated to endanger public health and welfare," and in the specific case of the welfare based secondary standard for ozone and other photochemical oxidants, require that the Administrator specify a level of air quality that "is requisite to protect the public welfare from any **known or anticipated** (emphasis by me) adverse effects associated with the presence of [the] pollutant in the ambient air."

The phrase "known or anticipated" provides both a significant degree of discretion, and a substantial responsibility for the Administrator to use prudent professional judgment in dealing with uncertainties and deficiencies in available scientific evidence regarding the effects of ozone and other photochemical oxidants on crops, forests, and natural ecosystems and their relationship to values held dear by the people of our country.

**3. <u>Air Quality Characterization (Chapter 2)</u>**

From the standpoint of *Policy Relevant Assessment of Welfare Effects Evidence* (and especially the effects of ozone on crops, forests, and natural ecosystems) as described in Chapter 7 of the Staff Paper, there are several important parts of the Air Quality Characterization section (Chapter 2) of the Staff Paper:

a) Definitions of the present identical primary and secondary ozone standards (8-hour) and the two distinctive cumulative secondary standards proposed for consideration by the Administrator in 1996 (SUM06 and W126) as discussed on pages 2-11 and 2-12;

b) Maps showing the distribution of county areas within of the US that exceed the present identical primary and secondary 8-hour standards (8-hour) and would exceed the alternative and cumulative proposed secondary standards as discussed on pages 2-13, 2-16, and 2-17;

c) Charts showing the duration of high-ozone episodes across the US on pages 2-35 and 2-38, and

d) Discussion of seasonal variability in ozone exposures on page 2-24.

The value of these various parts of Chapter 2 for understanding the major conclusions in Chapter 7 will be enhanced if more inter-chapter linkages and cross-references regarding exposures of crops, forests and natural ecosystems are included in the text of both chapters. It also will be valuable to include in chapter 2, a chart similar to those on pages 2-28 and 2-32 showing the diurnal patterns of ozone concentrations at a high-elevation forest site where ozone concentrations during nighttime hours frequently remain relatively high. These nighttime concentrations of ozone are important because of their injurious effects on high-elevation forests as discussed on page 7-22.

**4. <u>Relationships Between the Quality of Statements Scientific Findings in the 2005 First Draft Staff Paper and Related Statements in the Executive Summary, Main Chapters, and the Annexes of the 2005 Criteria Document on Ozone and Related Photochemical Oxidants</u>.**

As indicated in my verbal remarks during both the Peer Review of EPA's 2005 2nd Draft Ozone Air quality Criteria Document on Ozone and again during the Consultation on EPA's 2005 1st Draft of the Ozone Staff Paper and Technical Support Documents, my review of the assigned Vegetation and Ecosystems Effects parts of these two major documents was accomplished in four distinct steps:

a) My review began (as I thought appropriate at the time) with the 410 pages of Annex A9X in the Criteria Document titled *Environmental Effects: Ozone Effects on Vegetation and Ecosystems.* The principal focus of my review was on major conclusions and statements of scientific findings about ozone effects on vegetation as developed in the very detailed analyses within the Annex.

b) My review continued with the 21 pages of the Main Chapter (Chapter 9) that (appropriately) had the same title as the Annex A9X from which the major conclusions and statements of scientific findings in the Main Chapter were derived.

c) My review then shifted to the 4 pages of the Executive Summary (section E.9) titled *Vegetation and Ecological Effects*. Once again, major attention was given to the major conclusions and statements of scientific findings in the Executive Summary that were derived from the Main Chapter and their supporting evidence in the much more detailed Annex.

d) My review then culminated with careful study of the 63 pages of the vegetation and ecosystems effects part of the Staff Paper (Chapter 7) titled *Policy-Relevant Assessment of Welfare Effects Evidence*. Once again my attention was focused mainly on the major conclusions and statements of scientific findings as presented in the Staff Paper and their relationship with- and faithfulness to- the evidence presented in the three parts of the Criteria Document as described above.

In retrospect, as indicated in my verbal remarks during both the CASAC Peer Review and the separate Consultation on the Staff Paper on December 6-8, 2005, it probably would have been better if the order of my review had been reversed. Although the scientific content of all four documents are not in substantial conflict, some very important differences in scientific content were evident and the apparent objectivity and tone of the four documents were rather divergent. In general, I was more satisfied with both the tone and quality of statements of findings in the Staff Paper than in different parts of the Criteria Document.

The policy-relevant merit of this reverse order became even more obvious, in view of the written summary of carefully considered professional judgment I had prepared and presented directly to CASAC during the 1996 review of the Criteria Document and Staff Paper nine years ago. This written summary was titled "*Avoiding the Necessity for a Second NRC Report on 'Rethinking the Ozone Problem in Urban and Regional Air Pollution' during the Years Between 2002 and 2017."* A verbatim copy of this 1996 statement was included in my written comments dated April 29, 2005 and is included here once again as Appendix A for whatever value it may

have in the drafting of the 2nd draft of the Staff Paper, further revision of the Criteria Document, and maybe even in deliberations by the Administrator of EPA.

As indicated in written comments dated December 2, 2005 that I prepared prior to the CASAC Peer Review of the 2005 2nd Draft of the Criteria Document for Ozone on December 6-7, 2005:

> The Annex for Chapter 9 contains a very thorough and well-balanced summary of existing knowledge regarding the effects of ozone on crops, forests, and natural ecosystems. When comparisons were made between the scientific understanding obtained from the Annex and the Main Chapter, however, I was much less satisfied with both the content and objectivity [and tone] of the Main Chapter than of the Annex. Furthermore, when comparisons were made between the qualities and completeness of understanding obtained from the statements of scientific findings in the Executive Summary, still other important discrepancies of both content and objectivity [and tone] were observed. In fact, my confidence in the vegetation and ecosystem effects parts of the Criteria Document was partially restored during my review of the scientific content of the Executive Summary. But my concern about the objectivity [and tone] of the information presented in the Executive Summary remained high as discussed in the next paragraph.
>
> I very much favor the inclusion of an overall Executive Summary in the Criteria Document since it is likely to be the most often used part of the whole Criteria Document. I also believe that most of the text of an effective Executive Summary should take the form of carefully crafted statements of scientific findings that contain 'the distilled essence of present scientific and technical understanding of the phenomena or processes to which it applies.'" But it obviously is highly desirable that all three parts of the Criteria Document be substantially congruent with each other and that both the scientific content and the apparent objectivity and tone of the three sections be very similar.
>
> The new organizational format for organization of the relatively brief Main Chapters of the Criteria Document itself, and the more detailed Annexes, is a very good idea. It is also a very good idea to have an Executive Summary for the whole Criteria Document – one that summarizes key scientific findings and emphasizes new developments since the last Criteria Document. It is also a very good idea to continue the practice of providing detailed annexes that provide thorough analyses and interpretations of the large body of scientific information on which each Main Chapter is based.
>
> These two innovations in the overarching method of organization of this Criteria Document will better serve the interests of the wide variety of audiences that are interested to learn more about scientific understanding of ozone and related photochemical oxidants and their effects on both human health and welfare. Thus, I believe these two revisions in organizational structure should be retained **not only in the Final Draft of this Criteria Document** dealing with ozone and related photochemical oxidants **but also should be used in preparing Criteria Documents for other Criteria Pollutants.**
>
> In doing so, it is of course important that the different target audiences for the Executive Summary, the Main Chapters of the Criteria Document itself, and the various Annexes be very well defined and well understood by the staff, consultants, and editors that prepare these three different treatments of the same body of scientific knowledge.

It is even more imperative that the scientific content and objectivity [and tone] of the Executive Summary [and the Staff Paper as well!] be consistent not only with the scientific content, objectivity [and tone] of the main chapters of the Criteria Document itself, but also with the scientific content and objectivity of the more detailed Annexes. Differences in content of these documents should be based primarily on their relevancy to their respective purposes and target audiences. But discrepancies in either scientific content and/or objectivity [and tone] of these three distinct parts of the Criteria Document [and the Staff Paper as well!] will inevitably lead to decreased confidence in the validity and reliability of all three [or four] documents. Thus such discrepancies must be carefully avoided. This will require a larger degree of common understanding among authors, consultants, editors, and managers of the criteria document development process than I believe has been achieved to date.

One specific **suggestion for avoiding discrepancies in communication among Executive Summaries, Main Chapters, and more detailed Annexes is to require that the very same carefully-crafted summary statements of scientific findings are not only included (but also printed in bold-face type) within <u>all parts</u> of complex scientific assessment documents**. This editorial device is used in many high-quality National Research Council assessment reports that also deal with very complex policy relevant scientific issues.

I recommended in written comments on December 2, 2005 [and affirm here once again] that all **authors, consultants, editors, and managers engaged in the preparation of Criteria Documents [and EPA Staff Papers] take full advantage of- and use the attached published *"Guidelines for the Formulation of Statements of Scientific Findings to be Used for Policy Purposes."*** These guidelines, written in the form of checklist questions, were developed by the members of the Oversight Review Board of the National Acid Precipitation Assessment Program (ORB-NAPAP) to assist scientists in other environmental research and assessment programs in formulating statements of scientific findings to be used in policy decision processes. The distinguished members of the ORB who prepared these guidelines included: Milton Russell, former Assistant Administrator for EPA, Chauncey Starr, former Director of Research for the Electric Power Research Institute (EPRI), Tom Malone, former Foreign Secretary for the National Academy of Sciences, John Tukey, Distinguished Professor of Statistics at Princeton University, and Kenneth Starr, Nobel Prize Winner in Economics.

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## GUIDELINES FOR FORMULATION OF STATEMENTS OF SCIENTIFIC FINDINGS TO BE USED FOR POLICY PURPOSES

The following guidelines in the form of checklist questions were developed by the NAPAP Oversight Review Board to assist scientists in formulating presentations of research results to be used in policy decision processes.

1) **IS THE STATEMENT SOUND?** Have the central issues been clearly identified? <u>Does each statement contain the distilled essence of present scientific and technical understanding of the phenomenon or process to which it applies</u>? Is the statement consistent with all relevant evidence that is available in the published literature. Is the statement contradicted by any important evidence in the

published literature? Have apparent contradictions or interpretations of available evidence been considered in formulating the statement of principal findings?

2) **IS THE STATEMENT DIRECTIONAL AND, WHERE APPROPRIATE, QUANTITATIVE?** Does the statement correctly quantify both the direction and magnitude of trends and relationships in the phenomenon or process to which the statement is relevant? When possible, is a range of uncertainty given for each quantitative result? Have various sources of uncertainty been identified and quantified, for example, does the statement include or acknowledge errors in actual measurements, standard errors of estimate, possible biases in the availability of data, extrapolation of results beyond the mathematical, geographical, or temporal relevancy of available information, etc. In short, are there numbers in the statement? Are the numbers correct? Are the numbers relevant to the general meaning of the statement?

3) **IS THE DEGREE OF CERTAINTY OR UNCERTAINTY OF THE STATEMENT INDICATED CLEARLY?** Have appropriate statistical tests been applied to the data used in drawing the conclusion set forth in the statement? If the statement is based on a mathematical or novel conceptual model, has the model or concept been validated? Does the statement describe the model or concept on which it is based and the degree of validity of that model or concept?

4) **IS THE STATEMENT CORRECT WITHOUT QUALIFICATION?** Are there limitations of time, space, or other special circumstances in which the statement is true? If the statement is true only in some circumstances, are these limitations described adequately and briefly?

5) **IS THE STATEMENT CLEAR AND UNAMBIGUOUS?** Are the words and phrases used in the statement understandable by the decision makers of our society? Is the statement free of specialized jargon? Will too many people misunderstand its meaning?

6) **IS THE STATEMENT AS CONCISE AS IT CAN BE MADE WITHOUT RISK OF MISUNDERSTANDING?** Are there any excess words, phrases, or ideas in the statement which are not necessary to communicate the meaning of the statement? Are there so many caveats in the statement that the statement itself is trivial, confusing, or ambiguous?

7) **IS THE STATEMENT FREE OF SCIENTIFIC OR OTHER BIASES OR IMPLICATIONS OF SOCIETAL VALUE JUDGMENTS?** Is the statement free of influence by specific schools of scientific thought? Is the statement also free of words, phrases, or concepts that have political, economic, ideological, religious, moral, or other personal-, agency-, or organization-specific values, overtones, or implications? Does the choice of how the statement is expressed rather than its specific words suggest underlying biases or value judgments? Is the tone impartial and free of special pleading? If societal value judgments have been discussed, have these judgments been identified as such and described both clearly and objectively?

8) **HAVE SOCIETAL IMPLICATIONS BEEN DESCRIBED OBJECTIVELY?** Consideration of alternative courses of action and their consequences inherently involves judgments of their feasibility and the importance of effects. For this reason, it is important to ask if a reasonable range of alternative policies or courses of action have been evaluated? Have societal implications of alternative courses of action been stated in the following general form?:

> "If this [particular option] were adopted then that [particular outcome] would be expected."

9) **HAVE THE PROFESSIONAL BIASES OF AUTHORS AND REVIEWERS BEEN DESCRIBED OPENLY?** Acknowledgment of potential sources of bias is important so that readers can judge for themselves the credibility of reports and assessments.

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**Additional Comments of Dr. Ellis Cowling in Response to the Charge Questions for Chapter 7 in the Staff Paper:**

The following comments are focused on the specific CASAC "Charge Questions" raised in Karen Martin's letter to Fred Butterfield dated November 14, 2005. Please note in the paragraphs below, that Karen Martin's questions are written in **bold-faced non-indented paragraphs**, whereas my responses are written in indented paragraphs without bold type.

**1. To what extent is the presentation of evidence drawn from the ozone Criteria Document related to the various welfare effects considered in this review technically, appropriately organized and balanced, and clearly communicated?**

In general, I find the text and figures of Chapter 7 to be "technically sound" and generally "clearly communicated." The scientific findings described here also are reasonably congruent with the Criteria Document on which the Staff Paper is based. In fact, the tone and objectivity of the Staff Paper is superior in some respects to the presentation of the same scientific evidence in the Criteria Document.

With regard to the question of "appropriate organization and balance," however, as indicated below, I have offered some suggestions that may help facilitate EPA staff efforts to meet some information-organizational needs of the Administrator.

As indicated on page 1-1, the principal purpose of the Staff Paper is to "help 'bridge the gap' between the scientific review contained in the Criteria Document and the judgments required of the Administrator in determining whether it is appropriate to revise the National Ambient Air Quality Standards for Ozone and Related Photochemical Oxidants."

Thus, my comments below are focused mainly on the quality of linkages between scientific knowledge as described in the Criteria Document and Staff Paper especially with regards to the adequacy or inadequacy of the existing identical 8-hour 0.08 ppm primary and secondary standards intended to protect crops, forests, and natural ecosystems against adverse effects of ozone and related photochemical oxidants.

The most important general conclusions in both the Criteria Document and Staff Paper are well presented on pages 7-2, 7-3, 7-27, 7-28, 7-29, 7-34, 7-35, and 7-36:

1) Scientific research accumulated since the 1996 review has not fundamentally altered understanding and conclusions regarding ozone effects on vegetation and ecosystems.
2) In some cases recent research has expanded and clarified scientific understanding at the level of plant cell and tissue response; only a few studies have filled gaps and uncertainties since the last review.
3) There has been a small increase in research on interactions between elevated carbon dioxide and ozone on the productivity of forests, and expansion of data collection and analysis of ozone induced visible injury at US Forest Service biomonitoring sites.
4) Ozone effects research on vegetation in Europe has continued apace but with a shift from consideration of ambient exposure measurements to modeled ozone uptake in

the hope of developing an exposure index that can be used as a planning tool for the European Critical Levels approach.

5) Recent advances have been made in mechanistic process models and leaf and canopy flux models and have improved understanding of relationships between ozone impacts on vegetation and impacts on ecosystem structure and function.

6) It is important to characterize ambient air quality over broad geographical, mostly rural areas of the US where important crops, forests, and natural ecosystems are the dominant land cover but have very few ozone monitors. Thus EPA staff is now evaluating a variety of approaches for estimating potential ozone exposures in these non-monitored areas.

7) Currently, research is underway to reanalyze data from the National Crop Loss Assessment Network (NCLAN) database to recalculate the C-R functions in terms of an 8-hour average index.

8) County-level crop planting data will be obtained for each NCLAN crop and to use these data to create GIS maps of percent yield loss in each county in which they were planted.

9) In light of these and a number of other developments since the last review, EPA staff plans to update the previous review's crop risk and economic benefits assessments in order to evaluate the adequacy of the level of protection afforded by the present identical primary and secondary standards for ozone.

As indicated earlier, I find the text and figures of Chapter 7 generally to be "technically sound" and "clearly communicated." With regard to the question of "appropriate organization and balance," however, permit me to suggest that the additional major findings in chapter 7 be reordered in order to emphasize relevancy to the primary purpose of the Staff Paper – to provide information that is essential to determining whether it is appropriate or necessary to revise the present identical primary and secondary standards for ozone and related photochemical oxidants.

In my judgment the following overall sequence of major scientific findings will increase their usefulness as the Administrator considers the merit of a secondary standard for ozone that is different in form from the primary standard. Please note that these comments are suggested **only to guide the sequence of information provided and are not intended to materially affect either the science-content or tone of the generally very sound statements already presented in the text of Chapter 7.**

1) Effects of ozone on vegetation are widely regarded to be the most important air pollutant induced welfare effect of concern in the US.

2) Ozone is the most abundant and injurious photochemical oxidant that affects vegetation, even though injurious effects by PAN and hydrogen peroxide also have been reported on some species of plants.

3) Ozone causes visible injury and significant losses in yield of cereal grains and forage quality in many species and varieties of crop plants, many species of forest and shade

trees, and many vegetation components of natural ecosystems in all 50 states and all 10 EPA regions of the US.

4) In some vegetable and floral crops and a few tree species (such as spinach, cut and potted flowers, and Christmas trees) visible injury itself has a direct bearing on the market value of the saleable plant product.

5) In many cases, exposure to injurious concentrations of ozone increases the susceptibility of crops, forest trees, and natural ecosystems to further damage or even mortality caused by pathogenic and parasitic fungi and insects, as well as bacteria, nematodes, viruses, and abiotic stress factors such as drought, frost, and nutrient deficiencies.

6) Exposure to injurious concentrations of ozone also is known to affect various physiological and ecological processes including:

    a) Altering relationships with beneficial symbionts such as mycorrhizae,

    b) Inhibiting some translocation and nutrient storage processes,

    c) Interfering with various aspects of reproduction including seed production, and

    d) Accelerating various normal senescence processes.

7) The magnitude of economic losses due to ozone effects on the major cereal crops of the US were estimated in a wide-ranging and long-term series of studies by the National Crop Loss Assessment Network during the 1980s to be of the order of several billions of 1988 dollars.

8) Many species and commercial varieties of crop plants and forest trees show visible symptoms of injury and significant losses in yield at concentrations of ozone that are considerably lower (0.04 to 0.06 ppm of ozone) than the 0.08 to 0.12 ppm of ozone that are generally recognized to cause ill-health in people.

9) Very substantial genetically controlled variation in sensitivity to ozone exists in essentially all of the relatively few species of crop plants and forest trees that have been tested for genetic variation in ozone sensitivity. Thus, substantial genetically controlled variation in sensitivity to ozone very likely also exists in most species of plants.

10) Photosynthesis is inhibited in most species of crop plants and forest trees by ambient ozone concentrations of 0.6 ppm or more (hence the SUM06 suggested secondary standard for ozone proposed in the 1996 Staff Paper).

11) Photosynthesis also is inhibited in many species of crop plants and forest trees plants by ozone concentrations of 0.4 ppm or more (hence the AOT40 Critical Level for ozone widely used in the European Union),

12) The effects of ozone on plants are cumulative throughout the growing season rather than acute or chronic in their action on the metabolic systems of plants (hence both the cumulative SUM06 and W126 secondary standards for ozone recommended in the 1996 Staff Paper). For this reason, some plant physiologists and ecologists like

me are prone to assert, somewhat factiously, that: “Plants do not worry about a bad Tuesday, but they do worry about bad ozone seasons.”

13) The SUM06 seasonal cumulative statistic is calculated by summing all 1-hour ozone concentrations greater than 0.06 ppm. The W126 seasonal cumulative statistic is calculated similarly to the SUM06 statistic. The only difference is the weighting function. SUM06 has a weighting function that is 0 when the concentration of ozone is less than0.06 ppm and is 1 when the concentration is greater than or equal to 0.06ppm. The W126 statistic is a continuous, sigmoidal weighting function with an inflection point between 0.06ppm and 0.07 ppm. The results of the SUM 06, W126, and AOT 40 cumulative statistics are expressed in ppm hours. The present identical 8-hour 0.08 ppm primary and secondary standards for ozone are not cumulative. The daily maximum 8-hour values are found by first calculating running or moving 8-hour values for all 24 hours in a day. Thus the maximum 8-hour value for each day is found. On an annual basis, the fourth highest values are summarized over a 3-year period to determine if a violation of the identical primary and secondary ozone standards has occurred.

14) The present identical 8-hour 0.08 ppm primary and secondary national standards for ozone provide a larger measure of protection of plants from adverse effects of ozone than the formerly used identical 1-hour 0.12 ppm primary and secondary standards for ozone.

15) Not only are ozone effects cumulative within a given growing season, but there also are “carry-over effects” from one growing season to another in various perennial crop plants and long-lived forest and shade tree species.

16) Ozone enters plants through stomata on the surfaces of leaves. Thus ambient concentrations of ozone are less injurious to plants that close their stomata at night and those that hold their stomata closed during periods of drought.

17) Although ozone enters plants through stomata, many plants show more marked effects of exposure to injurious concentration of ozone on root growth than on shoot growth.

18) Although ambient ozone concentrations show a marked diurnal pattern of variation with highest concentrations usually occurring during afternoon hours and much lower concentrations during nighttime hours, this diurnal pattern is much less pronounced and sometime even lacking entirely in some high elevation forests and natural ecosystems.

19) In contrast to human health risks that almost always are much lower when people are inside buildings, may be differ between weekdays and weekend days, and are much greater for persons that exercise vigorously while at work or play out-of-doors, crop plants, forest and shade trees, and natural ecosystems all are exposed to ambient concentration of ozone in all daylight and nighttime hours of the day, in all seasons of the year, and even across multiple years or even decades in the case of long-lived perennials and forest and shade trees.

20) Broadleaved tree species are generally more sensitive to ozone than annual plants and to most coniferous (needle-bearing) tree species.

**2. To what extent does this first draft Chapter 7 appropriately take into account the range of views of the Panel Members that were expressed orally and in writing during and after the consultation of the Environmental Assessment Plan?**

In general, I am very pleased with the extent to which this draft of Chapter 7 is responsive to the range of views expressed orally and in writing during the consultation on the Environmental Assessment Plan.

As indicated earlier, the value of both Chapter 7 and Chapter 2 will be enhanced if more inter-chapter linkages and cross-references regarding exposures of crops, forests and natural ecosystems are included in the text of both chapters.

It also will be valuable to include in both chapter 2 and Chapter 7, a chart similar to those on pages 2-28 and 2-32 showing the diurnal patterns of ozone concentrations at a **high-elevation forest site** where ozone concentrations during nighttime hours frequently remain relatively high. These nighttime concentrations of ozone are important because of their injurious effects on high-elevation forests as discussed on page 7-22.

My principal disappointments with this first draft are that we will have to wait until the second draft of the Staff Paper before seeing even preliminary results from the economic analyses that EPA staff is currently conducting and the even more important **staff recommendations with regard to the secondary standard for ozone.**

**3. To what extent do the figures aid in clarifying the text? Should more or less information of this type be included in the second draft?**

Lack of figures -- and especially pictures and charts displaying the important and sometimes very severe impacts of ozone on crops, forest and shade trees, and natural ecosystems -- is a major shortcoming of this first draft Staff Paper. Pictures are indeed worth a thousand words (or more!)

It is very important that the 2nd Review Draft of this Staff Paper include illustrations that show:

a) The distribution of stomata on leaf surfaces, ideally also a paired set showing stomata open and stomata closed, and a diagram showing the structure of the stomata within the palisade layer of a leaf,

b) Crop plants or floral plants grown under different concentrations of ozone,

c) Differences in grain yield with and without exposure to injurious concentrations of ozone,

d) The greater effect of ozone exposure on root growth than on shoot growth,

c) A collage of pictures showing foliar injury that decreases economic value of various leafy vegetables like spinach, cut flowers, and Christmas trees, and most important of all:

e) Widespread ozone-induced mortality or ozone-and-biotic-pathogen induced mortality of different species trees exposed to ozone in some of the national parks, state parks, and wilderness areas in various parts of the US,

f) A picture of the cross-section of the stem of a tree showing differences in width of annual rings in trees grown with and without exposure to injurious concentrations of ozone, and, if possible, also, a cross-section showing the differential width of annual rings on the same tree during years when ozone exposures were high and ozone exposures were low.

Once again I also mention the desirability of including in Chapter 7, more maps and charts like those now included in Chapter 2 to illustrate the exposure of plants to ozone concentrations that are injurious to crops and forests in various parts of the US.

**4. To what extent does this draft recognize important sources of uncertainty associated with the various component analyses?**

In this connection, I was particularly pleased with the opening sentence of the **Summary** on page 7-22: "From the above discussion, several cautionary statements emerge that must be kept in mind when considering the most appropriate and useful concentration- or flux-based forms for characterizing the air quality that is associated with adverse vegetation effects."

The **gently cautionary tone** of this opening sentence and the discussion that follows is both appropriate and necessary. There are a lot of gaps and uncertainties in available knowledge about ozone effects on vegetation. But these deficiencies must not be exaggerated or over emphasized if serious consideration is to be given once again in 2006 to the 1996 Staff Paper recommendation of a secondary standard for ozone different in form from the primary standard.

In this regard, I am also pleased with the more gently cautionary tone in the description of uncertainties, deficiencies, and gaps of knowledge in the Staff Paper than with the less cautionary tone (although not with the substance) of the summary of scientific knowledge provided by the Criteria Document on which this Staff paper is based.

**5. While recognizing the lack of quantitative information on O3-related ecosystem effects, what are the Panel's views on the appropriateness of how this topic is addresses in this draft?**

It was very satisfying to review the relatively large section of Chapter 7 (pages 7-45 through 7-52) devoted to discussion of current knowledge of ecosystem condition and function and how ozone and related photochemical oxidants are either known or may reasonably be anticipated to alter some of the many functional attributes of ecosystems such as energy flow; nutrient, hydrological, and biogeochemical cycling; and maintenance of food chains.

Clearly this is an area of substantial scientific ignorance with respect to how ozone and related photochemical oxidants are affecting these various ecosystem functions and services.

Nevertheless, it is encouraging that:

a) A rather thorough and reasonably well-documented summary regarding ozone effects on ecosystem functions and services is provided in these several pages (7-45 through 7-52) of the Staff Paper;

b) EPA staff is initiating efforts to identify indicators of ecological condition whose responses can be clearly linked to air quality; and

c) Recommendations regarding research needs on air quality impacts on ecosystems in the recent National Academy of Sciences report on *Air Quality Management in the United States* are also noted in this section of the Staff Paper.

Appendix A

Avoiding the Necessity for a Second NRC Report on
"Rethinking the Ozone Problem in Urban and Regional Air Pollution"
during the Years Between 2002 and 2017

Statement by Ellis B. Cowling
University Distinguished Professor At-Large and
Professor of Plant Pathology and Forest Resources at
North Carolina State University
to the
Clean Air Act Scientific Advisory Committee (CASAC)
EPA Auditorium
Research Triangle Park, North Carolina
March 21, 1996

The objective of this written statement is to provide additional justification to CASAC for recommending to the Administrator of EPA, that a secondary standard for ozone clearly different in form from the primary standard should be promulgated in 1997. This justification is based on three fundamental premises:

1) As discussed in the EPA Staff Paper on the secondary standard for ozone, a longer term seasonal standard, which is cumulative in form will provide an addition measure of protection against the harmful effects of ozone on the many different species of crop plants, forest trees, shade trees, ornamental plants, and the thousands of other plant, animal, insect, and microbial species that make up the living components of all the natural and managed ecosystems on which the quality of American life depends.

2) A secondary standard different in form from the primary standard will also accelerate and improve the processes of public education about many aspects of the tropospheric ozone problem. These aspects include, among others, the following general ideas:

-- Contemporary ozone pollution causes significant harm to crops, forests, ornamental plants, and natural ecosystems in many parts of the United States.

-- Ozone pollution is a serious threat to the welfare of people and ecosystems in many rural as well as urban areas of our country.

-- Ozone and its chemical precursors are frequently transported from rural areas to urban areas and from urban areas to rural areas in many parts of the United States.

-- The air concentrations of ozone and other oxidants that cause harm to crop plants, forests, and natural ecosystems are appreciably lower than the concentrations of ozone and other oxidants that cause harm to most people.

-- Ozone pollution is not just an urban problem associated with high peak concentrations of ozone during exceptional weather episodes but also a problem of longer-term chronic

exposures of plants to much lower, but still toxic, concentrations under persistent weather conditions.

3) A secondary standard clearly different in form from the primary standard will also have significant and pronounced effects on the nature, quality, and policy relevancy of ozone-related scientific research that will be undertaken during 1997 and beyond. A very important objective of that research should be to:
-- fill the persistent gaps in available knowledge, and
-- decrease the continuing scientific uncertainties
that have plagued ozone decision making in the past and, if we do not change the way we think about the ozone problem, will continue to plague the periodic updates and CASAC reviews of the Ozone Criteria Documents that are now scheduled to occur in 2002, 2007, 2012, 2017, etc.

Every CASAC member is aware of the 10 principal findings of the 1991 NRC report entitled "Rethinking the Ozone Problem in Urban and Regional Air Pollution" and the call for reform of the precepts for decision making about tropospheric ozone that were advanced in Milton Russell's classic paper: Ozone Pollution: The Hard Choices (Science 241:1275-1276, 1988) -- see attached reprint.

The title-words Rethinking in the NRC report and Hard Choices in Milton Russell's paper were chosen very deliberately. The intent in both cases was to encourage a significant change in the way American scientists, regulatory officials in industry and government, and the public at large think about ozone pollution and its management. Without a radical change in the quality of scientific, regulatory, and public thinking, both the NRC committee, and Milton Russell, former Assistant Administrator of EPA, were convinced, the United States will continue to fall short of its own objective -- to develop robust, scientifically sound, and cost effective strategies and tactics by which to manage ozone pollution during the remainder of this century and beyond.

The NRC report of 1991 indicated that despite 20 years of expensive and well-intentioned attempts, America's efforts to manage ozone near the ground "largely have failed." These attempts failed for two primary reasons:

1) Because the identical primary and secondary ozone standards established in 1970-71 and in 1978-79 were neither statistically robust nor founded on an adequate scientific understanding of the biological, chemical, and meteorological processes that lead to ozone accumulation near the ground, and
2) Because previous decisions about the kinds and quality of ozone-relevant biological-effects research and atmospheric-science research that was done were too often driven primarily by short-term regulatory deadlines, and, frequently, by incomplete scientific perceptions and policy assumptions.

The time has come for American scientists, leaders in industry and government, and people in general to understand that the problem of ozone pollution can not be managed by continuing to believe that the people in metropolitan areas like Atlanta, Chicago, New York, and other urban and regional ozone non-attainment areas can "solve the problem" of urban smog and regional ozone exposures without understanding the regionality and the seasonality of both the

ozone problem itself and the regionality and seasonality of the management approaches that must be used if the nation is to learn how to manage ozone and other oxidants at reasonable cost.

This deficiency in understanding of the regionality and seasonality of the ozone problem was one of the most important points made in the NRC report and in Russell's "Hard Choices" paper. But these same deficiencies were driven home even more forcefully in November 1994, when 26 of the 29 states that were required to submit a State Implementation Plan for Ozone were unable to make an attainment demonstration following available guidelines.

As a result:

-- Mary Nichols issued her now-famous "Memo of March 2, 1995,"

-- The Environmental Commissioners of States (ECOS) joined together with EPA in creating the Ozone Transport Assessment Group (OTAG) involving more than 30 states east and some west of the Mississippi River, and

-- The Federal Advisory Committee Act Subcommittee on Ozone, Fine Particulate Matter, and Regional Haze Implementation was created to look at least three of the five or six air-pollution problems that are related to the general oxidative capacity of the atmosphere (the other problems being acidification of soils and surface and ground waters, nitrogen satuaration of forest soils, and airborne-nitrogen-induced eutrophication of surface waters).

But even these more recent initiatives are driven by unrealistically short-term regulatory deadlines, and, frequently, by incomplete scientific perceptions and policy assumptions. Examples include:

-- Use of specific exceptional ozone episodes rather than by both episodic and season-long ozone time periods of interest,

-- Use of local and regional emissions inventories for natural and anthropogenic emissions that are of uneven quality for both rural and urban/suburban sources of ozone precursors,

-- Use of emissions-based mathematical models rather than both emissions-based and observation-based air quality models, and

-- Use of models that may "get the ozone peaks right" but are not skillful enough to "get the peaks, and the low ozone concentrations, and the natural and anthropogenic ozone precursors right" at the same time.

As CASAC makes its decisions about the closure letter that must now be written about the secondary standard for ozone, I hope all committee members will think very carefully about the nature, quality, pace, and intensity of research interactions that will occur as the result of the two choices you will help make today:

1) To recommend, once again, that identical primary and secondary standards be established for ozone in 1997, as was done in 1970-71 and in 1977-79, albeit, an 8-hour primary standard for which CASAC already has prepared a closure letter; or, alternatively,

2) To recommend that a secondary standard clearly different in form from the primary standard be established -- an 8-hour primary standard of simple form, and a separate 3-month-long standard of cumulative form as recommended in the EPA Staff Paper.

I hope CASAC will reflect very carefully on the extent and thoroughness of rethinking of the ozone problem that will occur under these two alternative choices. How differently will the thinking and nature of communications be -- both between and among the following kinds of expert- and non-expert persons who are interested in or have responsibilities for research and management decisions about ozone pollution:

-- air pollution biologists,
-- atmospheric chemists and physicists,
-- air pollution meteorologists,
-- air quality modelers,
-- state and federal air-quality officials,
-- air-quality leaders in industry and commerce including those in:
    -- the utility industry,
    -- the automobile industry,
    -- the petroleum industry,
    -- the printing, painting, solvents, and forest products industries,
    -- etc.

and, perhaps most important of all,

-- the public at large who will ultimately pay the bills for whatever decisions are made about ozone management during the years ahead?

In Summary:

Promulgation of a secondary standard for ozone that is clearly distinct in form from the primary standard will accomplish five important things:

1) It will provide an addition measure of protection against the harmful effects of ozone on the many different species of crop plants, forest trees, shade trees, ornamental plants, and the thousands of other plant, animal, insect, and microbial species that make up the living components of all the natural and managed ecosystems on which the quality of American life depends.

2) It will accelerate and improve the processes of public education about many aspects of the tropospheric ozone problem and its management.

3) It will enhance and improve the nature, quality, and policy relevancy of the scientific research that will be undertaken during 1997 and beyond.

4) It will enhance the quality and intensity of interactions that will occur between air pollution biologists concerned with the impact of ozone on crops and forests and atmospheric scientists who are interested in the chemical, meteorological, biological, energy use, transportation, and industrial-development processes that undergird our future air-quality management policies; and

5) It will avoid the necessity for another NRC report on "rethinking the ozone problem in urban and regional air pollution" sometime during the years between 1997, 2002, 2007, 2012, and 2017 because we failed, once again in 1996 and 1997, to recognize the need for still further rethinking of the tropospheric ozone problem.

# Dr. William (Jim) Gauderman

Jim Gauderman
OAQPS Staff Paper (SP) – Draft 1 and
Ozone Health Risk (HR) Assessment – Draft 1

SP, Table 5-2, 5-3: Will the '---' be replaced by values in the next draft?

SP, Page 5-10, line 18: This is not quite accurate, since Equation 1 does not include multiplication by the number of people in the relevant population.

SP, Page 5-10, line 20: The term 'fractile' should be more clearly defined.

SP, Page 5-12, Equation 5-1 and HR, Page 3-4, Equation 3-1: This equation is unnecessarily complicated. You need only a single term that defines weighted average risk for a given distribution of exposures, which would have form:

$$R^*_{km} = \Sigma_j \, (R_k \mid e_{mj}) \, P(e_{mj}).$$

All terms here are as defined in Equation 5-1, except that I suggest you replace $P_j$ by the more explicit term $P(e_{mj})$, use R instead of RR to avoid confusion of this term as a relative risk, and add a '*' (or bar) on the left-hand side of the equation to make it clear that this quantity is an average risk. The added index 'm' denotes the assumed distribution of ozone (recent ambient, background ambient, etc.).

It is important for the reader to be able to understand the calculations leading up to the lung function response tables to a greater degree than is possible in the current drafts. I suggest expanding the text, or adding an appendix, that works through one calculation for a given city to demonstrate how each model input is used.

Risk estimates should be provided for 10% reductions in FEV1 in the staff paper, as is done in the risk assessment draft.

The use of a linear exposure-response function for the FEV1 calculations should be revisited. This has the undesirable statistical property of providing negative risk estimates at low exposures. A logistic function would be a good alternative. One could make the reasonable assumption that risk is negligible at ozone concentrations less than the PRB if additional data points are needed to fit the curve. At a minimum, a demonstration that the calculations provided in the current draft are relatively insensitive to the choice of linear versus logistic risk function would go a long way to reducing concern about the general use of the linear function.

# Dr. Henry Gong

Individual Review Comments for U.S. EPA Ozone AQCD (2nd draft).
Henry Gong, Jr., M.D., 12/4/05
CASAC Ozone Review Panel

RE: (1) "Review of the National Ambient Air Quality Standards for Ozone: Policy Assessment of Scientific and Technical Information." November 2005 (hereafter called OAQPS Staff Paper-1st Draft).
(2) "Ozone Health Risk Assessment for selected Urban Areas: Draft Report." October 2005. Abt Associates. (hereafter called Draft Ozone Risk Assessment)

OAQPS Staff Paper- 1st Draft
Chapter 5. Characterization of Health Risks.
General Comments
The chapter appears reasonable for risk characterization although I have two caveats:

a. I must request that my colleagues who are more experienced with risk assessment methodology to fine-tune this draft.
b. I would like clarifications about assumptions, unstated gaps, rationale for certain decisions, and applications (see below).

Specific Comments

1. The language in the initial 15 pages suggest that "uncertainty" and sources of uncertainty are rampant and might restrict further conclusions, let alone risk assessment. Can Staff be more implicit about the limits of certainties and uncertainties?
2. Page 5-5: The Staff decision to use lung function decrements associated with ozone exposures in children (ages 5-18 yr) is described. The lung function response is based on data from adults (18-35 yr). Does this mean that the risk assessment excludes (or ignores) lung function responses in adults?
3. Pages 5-5 to 5-7: The decisions to exclude respiratory symptoms in children in risk assessment and to dispute the use of inner city asthmatic subjects are problematic. Although children's symptoms may be difficult to interpret, the lack of new symptom reports since the 1996 review does not mean that this dimension is unimportant or lacking. Although I do not have a "solution" for the "non-publication" issue, this issue can be discussed and previous risk assessments with symptoms be revisited with the as is, just meeting, and alternative ozone standard scenarios. Asthmatic subjects living in inner cities constitute another important at-risk or sensitive group. If the original investigations show significant health effects, these should be somehow acknowledged, even at the risk of adding another assumption about baseline incidence data (page 5-7).
4. Page 5-8: The single season of April-September in 2004 is selected to represent as is air quality. I planned to ask why should a single year be used, in view of the known annual variability of ambient ozone. However, I am glad to see that 2002 air quality will also be evaluated (page 5-9).
5. Tables 5-2, 5-3, 5-4: These tables have numerous incomplete cells. Why? What do the dashes mean? I was very surprised to see that the total population of Los Angeles, Riverside, San

Bernardino, and Orange Counties is "---" (Table 5-2). The population numbers are based on the 2000 census. I assume that population projections (e.g., to 2010, when these revised regulations presumably take effect) would be acceptable, but then we would not have actual data for mortality rates and hospital admissions for future years.

6. Tables 5-5 and 5-6: Why are FEV1 decrements of 10% or greater not also calculated in these tables? The draft Ozone Risk Assessment document uses the 10% category. A 10% decrement may still represent a clinically significant change in an individual and in a large population and may represent a lower (?) bound. It is difficult to discern the differences between the two tables.
7. Tables 5-9 and 5-12: Rationale for using only this single reference? Aren't there other studies as well?
8. I am looking forward to the next draft in which the alternative ozone standards will be inputted. It would be helpful for the reader to have a summary table that compares the key outcomes with the different scenarios (side-by-side).

Draft Ozone Risk Assessment
Chapter 3
General Comments
This is a draft technical support document from Abt Associates and constitutes a foundation for Chapter 5 of the Staff's ozone paper. In some ways this relatively succinct version reads better than Chapter 5, but chapter 3 is shorter because it evaluates controlled human exposures only! (Chapter 4 evaluates the epidemiological bases for risk assessment.) As such, Chapter 3 contains much of the same or similar information as in Chapter 5 of the Staff Paper. Furthermore, my issues are similar to those I raised above for the Staff paper. I note some differences, e.g., FEV1 decrements of 10% or greater are used in the as is and current air quality scenarios.

# Dr. Paul J. Hanson

**Comments on the**
**Review of the National Ambient Air Quality Standards for Ozone: Policy Assessment of Scientific and Technical Information**
**OAQPS Staff paper –First Draft**

**Submitted by: Paul J. Hanson**
**Date: December 5, 2005**

Pages 2-3 to 2-7: Can some estimate of the magnitude of the biogenic emissions of VOC and NOx be provided in the context of the emissions from anthropogenic sources?

Page 2-41 line 14: Text is missing "Background estimates of??? hour…."

Chapter 7 Welfare Effects:

I found this chapter to be a well-crafted discussion of the need for a policy-relevant assessment of welfare effects. The staff did a good job of addressing some of the comments that were brought up during the consultation on October 3, 2005.

Virtually all of the citations that I wanted to look at were missing from the reference list. A detailed check of references cited needs to be done.

Page 7-4 lines 18 to 21: Dry deposition is also altered by the turbulence within OTCs.

Page 7-5 line 7: Consider changing the wording to "This exposure method may more closely replicate ambient environmental conditions…"

Page 7-7 lines 13 to 15: I'm not certain that we understand the mechanism for why ozone exposure leads to stomatal closure. Experimental data have simply demonstrated that stomatal closure is correlated with ozone exposures.

Section 7.2.2.5

Plants don't think and they are incapable of defending themselves. The wording of this section places too much emphasis on plants as proactive reacting organisms. Plants biochemical processes may appear to react to environmental perturbations and pollutant exposures, but it is important to realize that a plant's inherent ability to avoid, tolerate or compensate for pollutant exposures is limited. Plant populations may, however, evolve over time through selective pressures to appear better adapted to a given environment.

Page 7-10 lines 35 and Page 7-11 line 1: The wording "the cell must mobilize repair to overcome the injury" is wrong. A cell does not have to mobilize a repair system. The appearance of foliar injury following ozone exposure is evidence that repair often doesn't happen.

Page 7-12 lines 17 to 20: This is a very important statement.

Page 7-15 lined 11 to 14: This sentence would be easier to read if it was broken up. For example, 'The relative humidity of the ambient air has generally been found to increase the adverse effects of ozone by increasing stomatal conductance and thereby increasing internal ozone flux. Likewise, abundant evidence indicates that the ready availability of soil moisture results in greater sensitivity to ozone.'

Page 7-19 lines 7 to 8: Please explain Musselman and Minnick's conclusion in more detail. What do they mean by possible lower plant defense at night?

Page 7-23 lines 1 to 3: Rather than developing more and more complex indices of plant response to ozone exposure, I would rather see EPA transition to the use of mechanistic models and a consideration of the flux based approach.

Page 7-24 lines 20 to 23: Large deciduous canopy trees typically have larger rather than lower canopy gas exchange rates and higher uptake of ozone (e.g., Hanson et al. 1994). The opposite pattern reported by Grulke and others was for a conifer.

Page 7-38 Section 7.3.4: The section numbers cited within this paragraph appear to be wrong. I believe they should be 7.3.4.1, etc. Alternatively, those sentences within lines 23 to 28 could be deleted.

Page 7-44 Section 7.3.4.4: The proposed Ponderosa pine simulations provide information relevant for western forest, but are of little value in the Eastern United States. TREGRO has been developed for eastern forest species and a comparable effort in the east should be considered.

Page 7-48 lines 24 to 28: Would it be appropriate to point out that species whose seed production results from open pollination (the potential to continually regenerate new genetic material) would be less susceptible to diversity losses than species highly dependent on vegetative propagation for continued survival?

Section 7.4.2.1

Carbon sequestration needs a better definition for this discussion. Are the authors talking about net C fixation or long-term soil C accumulation?

Section 7.4.2.2

Leaf and forest full energy balance calculations will be required for the analysis of ozone effects on water resource issues. Ozone induced stomatal closure does not necessarily reduce water loss if concomitant leaf temperature increases increase the vapor pressure gradients across the leaf.

# Dr. Jack Harkema

Date: November 30, 2005

Subject: Comments on 1) the 2nd Draft of the Ozone Air Quality Criteria Document (AQCD), with emphasis on Chapter 5, and 2) 1st Draft Ozone Staff Paper (Chapter 3: Policy-Relevant Assessment of Health Effects Evidence)

From: Jack Harkema

1) 2nd Draft of Ozone AQCD
General Comments: The EPA staff and expert consultants to the NCEA-RTP have done an excellent job with this revision and incorporating into the 2nd Draft the comments and suggestions made by the CASAC review panel in May, 2005. The restructuring of the three volumes, focusing the main criteria document chapters on shorter interpretative evaluations of the recent literature, and placing more-detailed descriptive information in the annexes are good improvements and make the document more clear, concise and workable for the reader. The addition of the executive summary with the use of concise bullets characterizing key findings and conclusions from the main chapters also strengthens the document.

Comments on Chapter 5: I found this chapter well written and adequately researched. The chapter is well organized and provides enough detail of pertinent reported research since the last AQCD. The added figures clearly enhance the written text, but more descriptive figure legends are needed. The summaries and interpretations provided at the end of each subsection are also well done and informative. I have listed below a few specific suggestions, questions and minor editorial changes for the authors to consider.

In the introductory paragraphs of each of the subsections, it would be helpful to the reader and give added strength to the document if a few references are provided in the text for some of the key findings that are highlighted.

Page 5-4; lines 9-11 Sentence stating with *Further experiments* . . . needs to be revised to correct grammatical errors and redundancy.

Page 5-5; section 5.2.1.3 This is a good example were a few key references should be provided in the introductory paragraphs.

Figure 5-2 Abbreviations used in the figure should be defined in the legend. Do the highlighted components of *Lung Lining Fluid* always lie below the mucous layer as illustrated? Maybe this could be redrawn to more adequately reflect the text.

5-7; line 24 change *the model* to *this in vitro model*

Figures 5-2 and 5-3 have some redundancy. Maybe one figure incorporating the key information of both would suffice.

5-17; line 19 Is MLN defined? Check.

5-12; Information in lines 1 and 2 are repeated in lines 12 and 13. Delete the introductory sentence in 5.2.3.1 (lines 12 and 13).

5.2.3.2 This section nicely emphasizes the relative influence of C x T for ozone, but a few comments on episodic versus continuous regimens of exposure would also be helpful.

5-26; line 31 end of sentence. Not sure what is meant by *basal lung epithelial permeability*. Clarify.

5-27; line 31 I don't think it is correct that only ozone exposures ≥ 1 ppm induce mediators to recruit PMNs in the airways of exposed laboratory animals. For example, it has been reported that monkeys exposed to 0.15 ppm ozone for 6 days had neutrophilic rhinitis (Harkema et al. Am J Pathol. 1987 Jul;128:29-44). Be careful in your wording not to over generalize especially in reference to specific exposure concentrations and responses in laboratory animals.

5-36; line 25 Provide the strain of mice used.

5-38; line 19 Not sure where the . . . *0.15 ppm in rats and lower concentrations in primates* comes from. Check.

5.2.4.3 It may be helpful to add the figure by Dungworth illustrating tissue response and length of exposure (as found in the previous AQCD) to this document to complement the first paragraph of this section.

5-42; line 27 Add epithelial hyperplasia to the list of effects on nasal mucosa.

5-42; line 29 Fibrotic changes should refer to lung tissue.

The subsections on coexposures are nicely done.

5-77; line 23 Delete *of*.

2) 1st Draft Ozone Staff Paper (Chapter 3: Policy-Relevant Assessment of Health Effects Evidence)

General Comments:
Chapter 3 is very well written and adequately presents the evidence assessed in the Ozone CD. I found it to be clearly presented, technically sound, and appropriately balanced across the health effects areas.

I also found the tables very helpful in summarizing the ozone-induced health effects.

The staff's characterization of susceptible groups that may be more sensitive to ozone exposure also appears justified and clearly documented in this first draft.

Specific Comments:

3-23; line 8 The statement that *epithelial hyperplasia follows a somewhat similar pattern to ozone-induced inflammation is not true* and should be deleted or corrected. Epithelial hyperplasia peaks soon after the inflammatory response, but is usually maintained in both the nose and lung, with continuous exposure. Epithelial hyperplasia/metaplasia also does not quickly repair after the end of exposure. Interestingly, long-term studies in rodents suggest that inflammation is maintained in the nasal airways with chronic continuous exposure (Harkema et al. Am J Respir Cell Mol Biol. 1997 May;16(5):521-30).

It must be noted that chronic episodic exposures may not have this same pattern of zone-induced tissue response for inflammation, epithelial hyperplasia or fibrosis. It must be emphasized that the described progression of morphologic effects is based primarily on the results of long-term animal studies using continuous, rather than episodic, exposures. This is an area for future research.

3-21; line 19 In a study by Harkema et al. (Response of macaque bronchiolar epithelium to ambient concentrations of ozone; Am J Pathol. 1993 Sep;143:857-66) monkeys were exposed to 0.15 and 0.30 ppm for 90 days and had airway remodeling of the bronchiolar airways at both concentrations.

## Dr. Philip K. Hopke

Comments on the First Draft Staff Paper for Ozone
Philip K. Hopke

A major problem with this version of the SP is that it loses the focus on other photochemical oxidants. Chemistry in the atmosphere is almost exclusively photochemistry. It leads to the formation of oxidants including ozone that drive the concentrations of other species such as acids and particles. The purpose of regulating ozone is the overall control of photochemical oxidants. The breadth of the influence of photochemical oxidants is diminished too far by restricting the SP discussions to ozone. Control of photochemical oxidants including ozone and its reaction products would also provide controls on pollutants that include inorganic acids (sulfuric and nitric), particles formed from these inorganic acids, and secondary organic aerosols and their associated oxidants such as peroxides.

One of the key human exposure pathways for photochemical oxidants is the presence of reactive oxygen species (ROS) on the surface of particles such that a significant dose of oxidant is delivered to a small region of lung tissue in the vicinity of where the particle deposits. Gaseous oxidants like $O_3$ distribute their dose over the whole of the large lung surface such that the local dose in any specific location results in limited damage. Thus, the particle-bound ROS pathway may be key to understanding the toxicity of both ozone and PM. Note that ambient ozone has been found to be a better surrogate of ambient PM exposure than the PM itself. Thus, ignoring other photochemical oxidants may result in a considerable underestimation of the effects of photochemical oxidants.

In addition the role of ozone in the formation of secondary particles particularly secondary organic aerosol (SOA) is neglected in the document. Docherty et al. (2005) show that α-pinene and ozone produce particles with significant amounts of ROS. I strongly suggest that there is a significant added benefit in controlling ozone in that it will reduce the oxidant burden in the atmosphere leading to lower rates of formation of secondary inorganic (sulfate and nitrate) as well as organic particles. In particular, the organic particles can be the vehicles by which significant doses of oxidant to specific sites in the lung where deposition occurs.

It may not be possible at this time to fully quantify the benefits of controlling photochemical oxidants with respect to particle formation and particle-bound ROS, but these should at least be qualitatively be included in the Staff Paper. It is important to keep emphasizing the links between ozone, photochemical oxidants and secondary particulate matter.

It is time to evaluate the precision and accuracy of the current generation ozone monitors. These values feed into the rounding issue. It seems highly likely that we should now be rounding to the nearest 5 ppb instead of the nearest 10 ppb. However, there needs to be some precision trials. This should be easy to do in a time frame that would permit changes to be made in the final rule package. The rounding problem does represent a potential difficulty in terms of setting and

enforcing a standard that adequate protects public health and with a reasonable level of effort, this issue can be addressed straightforwardly.

The PRB discussion needs work and the use of the model results are uncertain. Rather than using the modeled daily PRB values to subtract from the daily measured values, the average diurnal values were estimated. The comments of Lefohn seem pertinent and need to be adequately addressed.

It is important NOT to move to a "never-to-be-exceeded" standard. As shown by Davidson and Hopke (1984), expected exceedances are quite unstable and the never to exceed standard would be even more statistically weak. There has to be opportunities for unusual convergences of atmospheric processes to lead to a limited number of high values. Appropriate protection for a percentile (or x allowed exceedances standard which is the same thing for complete data) can be obtained by setting the standard value lower. However, it is unrealistic to set never to be exceeded standards since it really requires the distribution to be shifted below the PRB levels given the closeness of the likely new standard level with the PRB.

With respect to the welfare effects, I did not see any staff recommendations with respect to a possible secondary standard with a different metric and this was disappointing in this first draft. The value of ecosystem function and services is inadequately presented. Although it is currently not possible to put a monetary value on ecosystems, they clearly play a major role in human experience. They provide recreational opportunities and aesthetic experiences that people value. They also provide critical support to human health and welfare. There does not seem to be adequate discussion of what would be appropriate exposure metrics that might include metrics for both cumulative exposure and the number of high value short-term exposures. I join the others on the panel who believe it is time that EPA demonstrates that it actually is committed to protecting the environment by setting an appropriate secondary standard for ozone.

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Davidson, JE, Hopke, PK, 1984. Implications of incomplete sampling on a statistical form of the ambient air quality standard for particulate matter, Environmental Science & Technology 18(8): 571-580.

Docherty KS, Wu W, Lim YB, Ziemann PJ, 2005. Contributions of organic peroxides to secondary aerosol formed from reactions of monoterpenes with $O_3$, Environmental Science & Technology 39 (11): 4049-4059.

# Dr. Michael T. Kleinman

**Michael T. Kleinman, Ph.D**
**December 16, 2005**

**OAQPS Staff Paper Chapter 3**

Charge Questions

$O_3$-related health effects (Chapter 3):
1. To what extent is the presentation of evidence assessed in the $O_3$ CD from the animal toxicology and controlled-exposure human experimental studies and epidemiologic studies, as well as the integration of information from across the various health-related research areas, technically sound, appropriately balanced, and clearly communicated?

The analysis is objective and technically sound.

2. What are the views of the Panel on the appropriateness of staff's discussion and conclusions on key issues related to quantitative interpretation of the epidemiologic study results, including, for example, exposure error, the influence of alternative model specification, potential confounding by co-pollutants, and lag structure?

See specific comments below

3. What are the views of the Panel on the adequacy and clarity of staff discussions on the issue of potential thresholds in concentration-response relationships?

I strongly support the statement on p.3-40

4. What are the views of the Panel on the appropriateness of the staff's characterization of groups likely to be sensitive to O3?

Neonatal and in utero exposure risks should be highlighted as new areas of research emphasis as these groups may be among the most sensitive and least studied.

General Comments

Overall this is a reasonably good summary, however there were some ambiguities in the way the material was presented. I have attempted to clarify some of the comments and to remove some apparent conflicts in statements. Also, some of the details that were made in the CD that provide important clarifications were left out in compressing the conclusions for this summary. The consistency of the Staff Paper with the CD needs to be carefully checked.

Specific Comments

| | |
|---|---|
| p. 3-5, l. 1 | Should this read “A characteristic of O3-induced inflammatory effect, ….” |
| p. 3-5, l. 3 | Some overall conclusion sentence should be inserted to be consistent with the rest of the paragraphs. |
| p. 3-6, l. 2 | Rather than “the decision” should you insert “the level and form of the standard”? |
| p. 3-6, l. 5 | Insert comma after “but supportive” |
| p. 3-7, l. 13-14 | Check that the actual number is three cases per million. This seems like and astonishingly small rate. |
| | Later it was mentioned that ER admissions were not used in the risk assessment because of uncertainty and small incidence numbers. This uncertainty should be indicated here. |
| p. 3-9, l. 18-19 | Should this read “reported at O3 concentrations as low as …? |
| p. 3-9, l. 19 | It would be better to be specific “(i.e. moderate rather than high level exercise)”. |
| p. 3-9, l. 30 | Change to “attenuation of responses. The attenuation is lost...” |
| p. 3-9, l. 36 | Change to “rest or with intermittent exercise (IE).” |
| p. 3-10, l. 12-13 | Change to “ statistically significant spirometric responses and increased symptoms with increasing duration...” |
| p. 3-10, l. 14 | Not sure what you mean by “total minute ventilation.” Do you mean average minute ventilation or total amount of air inhaled (i.e. CxV)? |
| p. 3-10, l. 18 | Insert comma “that, depending...” |
| p. 3-10, l. 20 | Change to “square wave exposures, when the overall O3 doses are equal”. This is more wordy but is more precise |
| p. 3-10, l. 21 | If the triangular exposure pattern results suggest that PEAK exposures are important in terms of O3 toxicology, than that point could be specifically mentioned here. |
| p. 3-10, l. 27 | Add-severe effects “that may be clinically as well as statistically significant.” |
| p. 3-11, l. 10 | “for the subgroup that reported having asthma and wheezing, and for those…” |
| p. 3-11, l. 17 | with a 30 ppb... |
| p. 3-12, l. 1 | attenuated even though at similar exposures pulmonary function changes might be attenuated. |
| p. 3-13, l. 3-4 | Delete “its” and insert “…ozone’s influence may have an immediate onset and may also persist…” |

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| p. 3-14, l. 6 | …though there was no… |
| p. 3-14, l. 7 | "…or inflammation…" |
| p. 3-14, l. 8 | …influence of the duration of exposure... |
| p. 3-14, l. 20 | Move section on in vitro study from 3-16, l. 2-5 to the end of mechanism paragraph. |
| p. 3-15, l. 6 | Mudway and Kelly (2000) instead of 2004? |
| p. 3-15, l. 16-21 | This paragraph could be in the section on mechanisms. ELF needs to be introduced and the role of oxidative stress needs to be explained before introducing this material. |
| p. 3-15, l. 36 | Is the use of the term respiratory region of the lung consistent with the language in the dosimetry section? |
| p. 3-16, l. 8 | Viral and bacterial? |
| p. 3-16, l. 26 | Be more specific about the differences in morphological effects (rats vs. primates) |
| p. 3-17, l. 34 | Given the toxicological evidence of fairly rapid resolution of ozone effects the rationale supporting the plausibility for the 30 day lag needs to be explained. |
| p. 3-18, l. 6 | …seen for O3-PM mixtures…? |
| p. 3-18, l. 19 | …collagen "possibly representing fibrotic changes." |
| p. 3-18, l. 25 | The sentence seems to imply that chest wall compliance and inspiratory capacity "increased" and that these were adverse effects. Was that the intent? |
| p. 3-19, l. 1-15<br>also p. 3-20, l. 1-19 | The paragraph relates to decreases in growth-related increases in pulmonary function. It might be better to use the phrase "growth-related increases" to avoid confusion. |
| p. 3-20, l. 29-32 | The results of the Sherwin study have limitations such as incomplete exposure data and smoking histories, possible confounding with other pollutants, etc. The limitations were mentioned elsewhere but should probably be restated here. |
| p. 3-21, l. 33 | Insert the limitations mentioned on 3-22 l. 1-3 here. |
| p. 3-22, l. 15 | Not sure what is meant by (no exposure metric given). Isn't it per ppb? |
| p. 3-22, l. 24 | Is there any reason to suspect that these healthy non-smokers are for some reason hypersensitive? The implication of the disclaimer is that a healthy lifestyle is setting us up for greater susceptibility to air pollution effects. Perhaps when this study stood alone the caution was warranted. However, there are other studies that imply similar findings so maybe the disclaimer can be softened. |

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| p. 3-22, l. 36 | Also point out that outdoor exposure duration was most likely greater for this group as well. |
| p. 3-23, l. 17-22 | These findings are more suggestive and far from definitive. If this is the "only epidemiological study" of morphological effects, it indicates that there is a clear need to do more studies in a formal rigorous way. |
| p. 3-25, l. 15 | It may be inappropriate to say that this group of studies "is generally inconsistent" because not all studies achieve statistical significance given that the trends in the data suggest an association. The issue of the warm season vs. the total year is legitimate, but there are adequate explanations in the CD. |
| p. 3-26, l. 33 | …higher temperatures are associated with the increased photochemical activities that are important for ozone formation… |
| p. 3-28, l. 27 | Is the issue really "decreased statistical power" or is it increased variance of the exposure-response relationship? |
| p. 3-28, l. 33 | Are the quantitative C-R functions missing from Dockery's paper or not presented in the CD? |
| p. 3-29, l. 27 | …report from the ACS study…? |
| p. 3-30, l. 10 | The associations are plausible; they may be given less weight in terms of evidence because of the small number of cases involved. |
| p. 3-31, l. 18 | Rather than saying "does not provide", could one say "is not yet sufficient to provide"? |
| p. 3-32, l. 30 | Change "approximately" to "appropriately"? |
| p. 3-33, l. 16 | There are several other potential sources of ozone indoors including air cleaners and any devices that have electrical motors that use commutators and brushes and produce sparks, including hair driers and vacuum cleaners. It might be useful to mention these as well. |
| p. 3-34, l. 12 | If the slopes are low, wouldn't the deltas be low also? Perhaps the statement in the text could be supported analytically. |
| p. 3-40, l. 35 | …attenuate over time, this does not mean that injury at the cellular and tissue level does not continue. Also, the time-line… |
| p. 3-41, l. 20-23 | The discussion of the Hatch study here does not carry forward from Chapter 5 of the CD the finding that if one considers the dosimetry, the sensitivity of rats and humans are consistent. The conclusion here may leave the impression that rodents are 5 times less sensitive than exercising humans and thus suggest that rodent data can not be used except in a qualitative sense. |
| p. 3-49, l. 17 | What is meant by the phrase "for negative seasonal effects"? |
| p. 3-52, l. 4,5,6 | Change "predicted" to "estimated" and define NL |
| p. 3-52, l. 29-30 | Do you mean "Ozone exposure leads to absorption of O3 in the ELF with |

subsequent depletion of ELF antioxidant level in the nasal ELF but concentration…"?

p. 3-53, l. 18 Insert "Also, children who participate in 3 or more outdoor sports activities have increased risk of developing asthma."

p. 3-67, l. 25-27 Perhaps this sentence should be copied to p 3-40, l. 35

Several possible research needs became evident on reading this chapter.

1. Rigorous epidemiological study of lung morphological changes that accounts for smoking Hx, exposure Hx, proper control groups, etc.
2. Re-analysis of long term epidemiology studies to examine the possible importance of peak exposures. This is stimulated by the difference between effects of triangular vs. square wave exposures.
3. Importance of indoor sources of ozone on overall exposure patterns.
4. Increased emphasis of in utero and neonatal exposure studies.

# Dr. Frederick J. Miller

**Dr. Fred J. Miller**
**December 16, 2005**

**Policy-Relevant Assessment of Health Effects Evidence**
**Chapter 3, OAQPS Staff Paper – First Draft**

**General Comments**

Overall, Chapter 3 represents a good start on an assessment of the health effects evidence to serve as the basis for characterizing the health risks in humans from exposure to ozone. The chapter could be shortened by less repetition of material from the CD. There are a number of areas where revisions are needed based upon technical aspects, interpretation of the existing data, and discussions during the CASAC Ozone Panel meeting. Some of these areas are listed below according to their appearance in the chapter:

- $FEV_1$ changes − Staff have focused on a reduction in vital capacity as the driver leading to changes in $FEV_1$. However, the pulmonary function changes with ozone exposure are driven by a reduced ability to inspire and then forcefully expel air such that IC and FVC are affected. Rewording of the discussion on this topic is needed.
- AHR − The statement that high exposure levels are required for AHR is not reflective of the CD comments wherein exposures to < 1 ppm ozone occur with agents that are bronchoconstrictive. More importantly, dosimetric adjustments need to be made before using the animal results to infer what might happen with any given human exposure.
- School absences − The studies in the CD on school absence are not sufficient to support this endpoint being one to feature in the list of effects caused by exposure to ozone. In addition, use of the Gilliland et al. (2001) study to support this endpoint is probably not warranted since the metric used in that study was a long term index, and there is not sufficient evidence that this duration of ozone exposure would lead to such changes in a "catch all" category like "all absence categories".
- Cardiovascular mortality − The case for cardiovascular mortality is overstated in the CD since only 4 of the 22 studies were statistically significant. In addition, the listing of studies in Figure 7-22 in Chapter 7 of the CD ranked according to increasing effect estimates tends to give a false sense of the strength of the association of ozone with this endpoint. That evidence from epi studies suggests some coherence in effects of short-term ozone exposure on the cardiovascular system is too strong a statement for Staff to make given the nature of the data base. For a NAQQS, greater magnitude and consistency should be required before one asserts any level of coherence.
- Threshold models for mortality − Staff's decision to not use a threshold model for ozone-mortality relationships needs to be revisited. Some studies discussed in Section 3.4.6 provide evidence for a threshold while others do not. Staff indicate that a population threshold is likely very low given some studies reported effects around 30 ppb. In view of the air monitoring data discussed at the CASAC AQCD meeting and the Staff Paper consultation, there is a need to consider a range of levels for what the Agency will consider as the Policy Relevant Background Level. Thus, all things considered, 30 ppb

for mortality analyses would clearly be the lowest value for a threshold based PRB. Other cut points (40, 50, 60 ppb) should probably be looked at for the acute mortality risk estimates. Not using a threshold model will tend to underestimate risks at higher exposure levels, although Staff present analyses indicating the difference is probably not a large one.

- Extrapolation models − All models are incorrect representations of "the truth" but some are useful – so Staff stating that extrapolation models have not been completely validated is begging the issue. Animal to human extrapolation can be done for a number of endpoints with sufficient accuracy to be useful in evaluating the potential for human effects (e.g., the amount of protein in lavage fluid).
- Outdoor workers − As did the CD, Section 3.6.2 of the Staff Paper First Draft fails to identify and discuss outdoor workers as a subpopulation that likely at increased risk from exposure to ozone. These individuals are outdoors for long time periods, engage in tasks that require moderate to heavy exertion, have increased ventilatory levels, and are likely to have repeated exposures over long periods of time. To this reviewer, these individuals are at significant risk, and the subset of outdoor workers having pre-existing respiratory disease (asthma, smoking, etc.0 are at even greater risk.
- Underlying Inflammation – Staff state that $FEV_1$ changes that would interfere with normal activity for relatively few sensitive individuals when the suffered $FEV_1$ decrements $\geq 10$ but $< 20\%$. have been judged to moderate. This reviewer would consider such changes adverse since even in healthy individuals we know that underlying inflammation is also occurring.

**Specific Comments**

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| p. 3-2, l. 25 | Very little new dosimetry information on ozone is available from animal studies. The vast majority of the new information comes from bolus studies using human subjects. |
| P. 3-3, 10 | Change "which" to "that". This incorrect use of "which" appears repeatedly throughout the chapter. |
| p. 3-3, 21 | Staff should point out that mechanistic data will almost always be only from animal studies. Staff should also discuss mode of action since the Agency is attempting to harmonize cancer and non-cancer methodologies for assessing risk, at least relative to the reliance on mode rather than mechanism leading to effects. |
| p. 3-3, l. 30 | Alteration in breathing pattern should be added to the list of changes imparted by exposure to ozone. |
| p. 3-4, l. 13 | In this section, the emphasis should not be on a reduction in vital capacity. The pulmonary function changes with ozone exposure are driven by a reduced ability to inspire and then forcefully expel air such that IC and FVC are affected. This is what leads to changes in $FEV_1$. This section could use some rewriting. |
| p. 3-6, l. 27 | This sentence is not needed as you just told the reviewer this a couple of sentences earlier. |
| p. 3-7, l. 25 | Is there some reason that staff want to list several lines of references instead of referring to the appropriate section in the CD? |

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| p. 3-8, l. 2 | Rewording is needed because the current sentence implies that the CD is a living entity! This type of revision may be needed in other places in the Staff Paper. |
| p. 3-8, l. 4 | As opposed to emergency department visits, the CD does not make it clear that the studies on hospital admissions have corrected for temperature and other weather variables. Staff should check that the papers they are relying upon did indeed make these kinds of adjustments. This is probably the case for those studies that did seasonal analyses. |
| p. 3-13, l. 17 | The statement that high exposure levels are required for AHR is not reflective of the CD comments on page 5-48 wherein exposures to < 1 ppm ozone occurs with bronchoconstrictive agents. In addition, dosimetric adjustments need to be made before the animal results should be inferred to have a bearing on human exposure effect levels. |
| p. 3-15, l. 2 | This would be an appropriate place for Staff to note that outdoor workers are likely to experience 8 h exposures with moderate to heavy ventilatory levels. |
| p.3-16, l. 4 | This statement about inherent sensitivity of cells from asthmatics compared to those from normal individuals is too strong. The in vitro study that is the genesis of this statement does not necessarily cross over to the in vivo situation. |
| p. 3-16, l. 12 | Staff should clarify that the few new studies is specific to alveolar macrophage phagocytosis and not to human studies in general. |
| p. 3-17, l. 13 | Staff should cite what “little evidence is available from human studies”. This reviewer is not aware of any structural studies in humans that would fall into this category being discussed for animals. |
| p.3-17, l. 33 | Use of the Gilliland et al. (2001) study on school absences is not warranted as the metric used was a long term index, and there is not sufficient evidence that this duration of ozone exposure would lead to such changes in a “catch all” category like “all absence categories”. The studies in the CD on school absence are not sufficient to support this endpoint being one to feature in the list of effects caused by exposure to ozone. |
| p. 3-19, l. 14 | Smaller increases compared to what? Please clarify. |
| p. 3-21, l. 1 | The data for long-term exposure effects on lung function in humans should probably be classified as “extremely weak” rather than “generally inconclusive”. |
| p. 3-21, l. 33 | Add a "s" to “eosinophil”. |
| p. 3-22, l. 12 | Should be “they enrolled” and not “the enrolled”. |
| p. 3-22, l. 14 | “A statistically ……” is not a sentence. |
| p. 3-28, l. 24 | This reviewer believes the case for cardiovascular mortality is overstated in the CD since only 4 of the 22 studies were statistically significant. In addition, the listing of studies in Figure 7-22 in Chapter 7 of the CD ranked according to increasing effect estimates tends to give a false sense of the strength of the association of ozone with cardiovascular mortality. One would think (as noted by Dr. Vedal’s |

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| | comments on the CD) that cardiovascular hospitalizations would show some relationship if cardiovascular mortality is really affected. |
| p. 3-30, l. 11 | Do U.S. Veterans generally have a lower life expectancy than the rest of the population? If they do, this could shed light on the apparent deviation this study represents from the rest of the long-term mortality studies for ozone. |
| p. 3-32, l. 26 | Check the page references to the CD here and throughout the staff paper. For example, mortality is not discussed on 7-45 or 7-46. |
| p. 3-33, l. 18 | Staff should also include the level of activity here since this factor determines the delivered dose of ozone respiratory tract lining fluids and tissues. |
| p. 3-35, l. 23 | Strike the word “be”. |
| p. 3-35, l. 28 | This reviewer concurs with Staff’s strategy of when to use single pollutant and multi-pollutant models. |
| p. 3-36, l. 4 | Insert the word “to” between “difficult” and distinguish”. |
| p. 3-37, l. 20 | In fact, the current epi studies for ozone do not lend themselves to any comments on temporality because various lag-structure analyses can not provide a true assessment of temporality. |
| p. 3-38, l. 5 | A left hand parenthesis is needed before “CD”. |
| p. 3-40, l. 10 | This reviewer does not agree with Staff’s decision to not use a threshold model for ozone-mortality relationships. Some studies discussed in Section 3.4.6 of this draft Staff Paper provide evidence for a threshold while others do not. Staff indicate that a population threshold is likely very low given the studies that reported effects around 30 ppb. An expanded higher range for the Policy Relevant Background level should be considered in view of the monitoring data presented at the CASAC meeting December 6-8, 2005. |
| p. 3-41, l. 19 | All models are incorrect representations of “the truth” but some are useful – so stating that extrapolation models have not been completely validated is begging the issue. The point is that animal to human extrapolation can be done for a number of endpoints with sufficient accuracy to be useful in evaluating the potential for human effects. For example, the amount of protein in lavage fluid shows a striking relationship when interspecies dosimetric adjustments are applied to the individual species and exposure studies. |
| p. 3-48, l. 29 | One can not jump from ozone reactions with cholesterol in surfactant lining the alveolar region to effects on the cardiovascular system. There is currently no evidence that these reaction products get outside of the lungs. |
| p. 3-49, l. 3 | That evidence from epi studies suggests some coherence in effects of short-term ozone exposure on the cardiovascular system is too strong a statement given the nature of the data base. For a NAQQS, greater magnitude and consistency should be required before one asserts any level of coherence. |
| p. 3-50, l. 26 | Are Staff arguing that the 20% of the U.S. population with impaired lung function is made up entirely by the percentage that have COPD, |

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| | asthma, or fibrotic lung disease? Impaired lung function reflected in $FEV_1$ decrements is likely in obese individuals, and obesity of the population is becoming recognized as a major public health issue. |
| p. 3-53, l. 1 | As did the CD, the Staff Paper First Draft fails to identify and discuss outdoor workers as a subpopulation that is most likely at increased risk from exposure to ozone. These individuals are outdoors for long time periods, engage in tasks that require moderate to heavy exertion and also increased ventilatory levels, and are likely to have repeated exposures over long periods of time. To this reviewer, these individuals are at significant risk, and the subset of outdoor workers having pre-existing respiratory disease (asthma, smoking, etc.0 are at even greater risk. |
| p. 3-53, l. 21 | In this section, numerous references are made to asthmatics. Since asthma is now considered a syndrome rather than a specific disease, the question arises as to whether the studies that have been conducted pinpoint a specific subtype of asthmatics. The answer to this question has important implications for any risk assessment estimates because the affected group may not in actuality be "anyone with asthma". |
| p. 3-58, l. 5 | "falling" not "fall" |
| p. 3-58, l. 15 | To this reviewer, the case for this sentence was already strong for the 1997 review of the ozone NAAQS and is even stronger now in light of the recent non-human primate studies. |
| p. 3-58, l. 28 | Add "in" after "decrements". |
| p. 3-58, l. 32 | Strike both uses of "below". |
| p. 3-58, l. 33 | Who did the judging when stated on this line ".., it has been judged that moderate …."? The statement is made in reference to changes that would interfere with normal activity for relatively few sensitive individuals when the suffered $FEV_1$ decrements $\geq 10$ but $< 20\%$. This reviewer would consider this adverse even in healthy individuals because we know that underlying inflammation is also occurring. |
| p. 3-68, l. 20 | What do Staff mean by "interspecies differences in sensitivity to chronic effects of O3 continue to be a limiting factor in extrapolation of effect responses in animals to human health effects"? There is a dosimetric difference that can be adjusted for and there is evidence from an autopsy study (as noted in the following paragraph) that permanent changes in lung structure occur in both animals and humans. |
| p. 3-69, l. 29 | This reviewer does not agree that specific factors contributing to the intersubject variability have not been identified. Both experimental dosimetry studies and mathematical dosimetry modeling have shown the importance of anatomical dead space volume in determining the delivered dose of ozone to the lower respiratory tract of animals and humans. In addition, genetic susceptibility studies have identified an important factor related to responses to ozone exposure. |

**Dr. Fred J. Miller**
**December 5, 2005**

## Chapters 4-6, OAQPS Staff Paper – First Draft

### Specific Comments

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|---|---|
| p. 4-1, l. 31 | The next draft should also present an assessment for healthy adults working outdoors at moderate to heavy minute ventilations for 6-8 hrs per day. |
| P. 4-11, l. 12 | Unless one assumes that all of the ozone is depleted during the simulation time interval, mass balance dictates that the concentration in the microenvironment at the end of the previous time step be accounted for. Why is this ignored in APEX? |
| p. 4-12, l. 17 | Ten occurrences for one person has much more significance than one occurrence for each of 10 persons. This reviewer is encouraged that Staff indicated the information is contained within the model to break this information down better. |
| p. 4-15, l. 30 | Given the age of some of the diaries, a major research need is to conduct studies that will yield more current data. Certainly activity patterns have changed over time. |
| Table 4-8 | The entries in this table for number of persons undergoing at least one daily maximum 8-hour average exposure should be rounded to whole numbers. This review seriously doubts the accuracy is to the tenth of a person and more importantly, part of a person is a non-sequitor. |
| p.5-6, l. 22 | I would not develop risk estimates for cardiovascular mortality. The lack of an increase in cardiovascular hospitalizations detracts from the coherence of the story for this endpoint. Moreover, since cardiovascular mortality dominates total mortality, one must question about providing any mortality risk estimates |
| p. 5-28, l. 24 | I still do not see why the bias must be towards the null. |
| p.5-30 | Section 5.4 on ozone risk estimates is difficult to follow because so many numbers and scenarios are discussed. Staff should seek to represent these data in a more condensed form. It might also be useful to give the bottom line at the beginning of the section prior to explaining all of the results. |
| p. 6-17, l. 9 | The dosimetry models can be exercised for the animal studies and then exposure scenarios leading to comparable doses in humans to the distal lung can be established. There is no reason this can not be done now, at least to obtain a reasonable range of human exposures that should be considered. |
| p. 6-17, l. 15 | For the form of the standard, why not consider a moving average of x days before computing the nth highest maximum concentration? This would provide protection against repeated occurrences in a short time period and still guard against allowing high levels of ozone to occur. |
| Fig. 6-1a,b | Shouldn't the evening symptoms estimate be greater than the morning estimate if ozone levels increase during the day and then first decrease in the evening? The legends need more explanation. |

# Dr. Maria Morandi

Exposure Analysis (Chapter 4 of the draft $O_3$ Staff Paper and draft Exposure Analysis technical support document) and Ozone Population Exposure Analysis for Selected Urban areas – Draft Report

Comments - Maria Morandi

In general, the approach is state of the art in probabilistic exposure modeling and combines accepted ambient air pollution models with residential characteristic and personal activity variables that impact exposure. As with any model that incorporates a broad range of input variables, uncertainties are inherent to the validity of the model assumptions and the quality and comprehensiveness of the input data. The limitations of the data are fairly well described. The assumptions of the model need to be stated clearly and upfront.

General suggestions

1. Chapter 4 and the rest of the Report do not consistently use the term exposure as defined in the earlier part of the Chapter, and sometime replaces what should be intake or dose, (which includes ventilation rate as estimated from METS)

It would be useful for the Agency to provide a brief summary of policy relevant research needs at the conclusion of the exposure chapter. Such summaries call the attention of the research community so it may provide impetus for obtaining relevant data for the next review. Examples include: 1) time location and activity levels of asthmatic children by age range; 2) distribution of ozone concentrations inside homes as a function of household activities and ventilation regimes, and 3) need for PEMs with lower MDLs.

In terms of the APEX model, state clearly the assumptions of the model as they relate to estimation or outdoor concentrations. The discussion of uncertainties is useful but they do not provide a sense of the boundaries for potential errors.

Answers to charge questions

1) To what extent is the assessment, interpretation, and presentation of the initial results of the exposure analysis in Chapter 4 technically sound, appropriately balanced, and clearly communicated?

The Chapter does a good job of presenting clearly the major findings of the Report in terms of variables that impact exposure. The Chapter would benefit from having a section (at the end) not only summarizing the major sources of uncertainty in the estimates but given some sense of bounds for the errors.

2) Are the methods used to conduct the exposure analysis technically sound? Does the Panel have any comments on the methods used?

There are some concerns, mainly introduced by assumptions because of methods and/or data limitations:

a) In conventionally air conditioned homes, ozone concentrations can easily be below the MDL of the instruments used as personal monitors in the studies cited by this document, essentially imposing an instrumental left censoring bias in indoor ozone concentration distributions, and consequently, exposure estimates.

b) Interpolation procedures for estimating ozone concentrations are of some concern because of the size of the grid and the presence within the grids of features that tend to titrate ozone (e.g., near roads). In addition to ground-level ozone concentrations profiles, there are some cities (e.g., New York) where there should be a consideration of vertical ozone profiles because of the density of apartment buildings and the street canyon effects. This issue and its implications should be discussed, if not addressed directly.

c) Using just the proportion of homes with AC as the infiltration-related critical variable for determining ozone penetration in residences is that having an AC system or unit does not necessarily mean that it is used. For economic reasons, residents may decide not to turn their AC on unless heat/humidity conditions become extreme, or they may choose to use AC only during certain times of the day or night. The lack of information on AC use (as opposed to AC presence) patterns could potentially impose a low bias in estimates of exposure for individuals living in air conditioned homes. Further, the bias introduced by the lack of a "use" factor could be associated with income level, specific meteorology of the city (i.e., more extreme conditions in Houston and less extreme in LA), and the comparative cost of energy in the various cities (electricity is less expensive in Houston, for example, than in New York). Since income and ethnic origin are associated, the low bias would be preferential for some ethnic groups. Some of the databases used to derive exposure estimates have information on socioeconomic factors and actual use of AC, so it may be possible to derive some estimates of such use from these data. It may also be possible to obtain information on energy use by census track from utility companies that could be utilized for partially accounting for the bias.

d) The upper limit of detection for AER estimated from tracer methods is approximately 5/hr, but an upper bound of 10 is used in the Report. Above an AER of 5/hr, the assumption of steady state concentration of the tracer is no longer applicable, and thus AERs above this level cannot be considered different. This needs to be explicitly recognized. In addition, there is no consideration of AERs for homes with evaporative coolers, which are frequent in the Southwest and parts of California The air exchange rates in this case can be quite high (up to 50/hr). There is an unpublished small study comparing indoor ozone concentrations in homes with evaporative coolers in El Paso and conventional AC units in Houston demonstrating that the residents of El Paso homes have higher exposures than those in Houston, because the I/O ozone ratios in the former can be 0.7 and <0.10 for the latter. At any rate, the cities selected will not represent all urban areas in the country.

In the case of buildings, an upper bound of 13+/hr appears excessive for mechanical ventilation. Since make up air in mechanically ventilated buildings can be set, and buildings are frequently not operated at optimum ventilation conditions (i.e., lower ventilations rates of make up air reduce energy costs), it is unlikely that the ventilation rates could be that high.

3. Are the exposure analysis methods and results fully and clearly communicated in the draft Exposure Analysis technical support?

Yes. They are.

4. To what extent are the uncertainties associated with the exposure analysis clearly and appropriately characterized in both Chapter 4 and the draft Exposure Analysis technical support document?

The sources of uncertainty are summarized appropriately. The question, however, is if the distributions derived for the various variables used to estimate exposure and intake incorporate those uncertainties.

5. What are the views of the Panel on sensitivity analyses that should be conducted to evaluate the influence of uncertainties in the exposure analysis?

Sensitivity analysis needs to be done in order to identify the critical data needs for improving exposure estimates.

Editorial (Exposure document-cross check with Staff paper)

Page 4-3 – Line 21. Change “Simplistic models” to “Simpler models...”

Page 4-5 – Lines 12-20. It would be useful to add a couple of reference on indoor ozone chemistry. (for example: Weschler CJ, Ozone and indoor environments: Concentrations and Chemistry, Indoor Air 10(4), 2000, which is cited later in page 4-15, and Monn C. Exposure assessment of air pollutants: a review on spatial heterogeneity and indoor/outdoor/personal exposure to suspended particulate matter, nitrogen dioxide and ozone, Atmos. Env. 35(1), 2001)

Page 4-5 – Lines 21-24. It should be mentioned that that increasingly popular ionic cleaners directed at controlling PM can generate significant amounts of ozone.

Page 4-15. Lines 15-19. While it is correct that indoor air reactions are slower than photochemically-driven outdoor chemical reactions and, therefore, decay would be a more important factor, this does not necessarily imply that ozone reactions indoors may not be as important or more in modifying exposure during certain activities of the residents (e.g., while cooking with a gas stove or using terpene-containing cleaners). The paragraph should be made less categorical on the issue of the importance of indoor ozone chemistry.

Page 4-17. The selection of 5 years as the lower age bound for school-age children needs to be reconsidered. Many urban school districts require preschool for ½ day at age four (some even at 3 years of age!)

Verify cross-references between staff document and the CD.

# Dr. Armistead (Ted) Russell

Review of the OAQPS Staff Paper – First Draft

Armistead (Ted) Russell

The comments below deal primarily with chapter 4 dealing with Characterization of Human Exposure to Ozone

Chapter 4 lays out how OAQPS estimated ozone exposure in 12 urban areas in the US. The twelve areas were chose to characterize across the U.S. in non-attainment regions. Their choice of areas is reasonable, encompassing areas in each of the regions where non-attainment is currently an issue. A bulk of the chapter deals with the application of APEX, the model they use to estimate exposures both currently, and in the future. They also discuss additional issues such as defining exposure, and personal exposure modeling, how data that drives APEX has been obtained, etc.. The chapter is derived largely from Chapters 2-4 of the "Ozone Population Exposure Analysis for Selected Urban Areas" report, reviewed separately

In general, APEX appears to be an appropriate model for use in this application. In its application, a number of choices need to be made, but in the base application, and in the future year exposure estimation as well (i.e., meeting the current standard). There will, of course, be some uncertainty as to how well APEX estimates exposure given that it is built up from a limited set of diaries (though, the number of diaries is quite large). The level of such uncertainty is not provided, but would be of interest. How does it compare with other estimates? The lack of a critical uncertainty assessment is probably the greatest weakness of the current chapter. They promise a sensitivity analysis as part of a future draft. This should be extended to be both a sensitivity and uncertainty analysis.

They have also run APEX for just 2004, a relatively mild ozone year, as acknowledged. 2002 will be modeled as part of the sensitivity analysis to be included in the next draft. EPA statisticians have developed a number of techniques to provide ways to deal with both high and low ozone years, and this should be considered here, i.e., answer the question of what would happen over a typical three year period, and what are the likely extremes (using different averaging periods).

The approach to simulate what happens to exposure when they meet the "Current Standard" needs to be better detailed. How, exactly, are the ozone levels adjusted. They note they use a quadratic model. What coefficients do they use in the quadratic for each city? Their approach to roll back concentrations does not use the PRB, but one might view that they should. They currently refer to Table 4D-1 to have the PRB, but that just contains the grid cells from GEOS-Chem. Table 4D-1 should be extended to give the PRB, its distribution, and all of the needed information to adjust to "Current Standard" for that city (e.g., the coefficients in the quadratic model). While the quadratic method is described in an attachment, greater detail is needed in the chapter. Also, given that the analysis is being done in a probabilistic fashion, the PRB should also have a distribution. Should there be any interaction between a probabilistically-defined

PRB and ozone values used in APEX? Given that there is an anti-correlation between peak ozone and PRB, this could modify the exposure estimate under the "Current Standard" rolled-back levels, e.g., how ozone is rolled back.

Another issue of interest is in rounding. The instruments in the field are better than two decades ago, and the use of a longer averaging time both suggest that the same magnitude of rounding is inappropriate.

4-23-16 The wording relating to the 20 x 20 km grid is ambiguous. Do they mean that the one grid is 20 x 20 (which does appear to be the case) or that they have a gridded domain that is 20 x 20 km, with finer grids inside. Next, how is this grid located, specifically, as the way it is left here, the origin is unknown. How sensitive are their results to the choice of grid?

Where does staff come down in terms of rounding? If one is to interpret the standard in one fashion, then how one adjusts concentrations should be done similarly. At this point, particularly using an 8-hr standard, and the 4$^{th}$ highest value, EPA should address if the precision of the instrument warrants not rounding to the nearest pphm. Also, is it protective to err on the high side? How would this affect the adjusted exposure estimates?

Appendix 4B: These graphs need to be better explained. Also, on the graphs starting at 0.00 ppm, how can the frequencies at 0.00 not be equal between the two cases? Also, they need to define frequency in the cases used.

Appendix 4C: Again, more explanation is needed within the appendix.

In direct response to the charge questions:

1. The analysis appears to be technically sound, but biased, since they are using a relatively low ozone year. Conducting the analysis using 2002 air quality is certainly needed. Aspects of the chapter need to be more clear, e.g., how the values are adjusted to "Current Standard". More explanation as to what the graphs in 4B and 4C represent would be valuable. At present, the major deficiency is the clarity and the need for greater detail.
2. They appear sound. As noted, the PRB might also be represented as a distribution. They should note that there is a negative correlation between PRB and ozone level. There is a need to provide an evaluation of APEX, if possible, for a some test case.
3. The review of the draft Exposure Analysis is done separately, but the answer is that that document is not clear. See below.
4. This document is non-quantitative in terms of uncertainties, which is a major weakness. They identify areas of uncertainty, but without some quantification, it is impossible to discern what are the main uncertainties and how they would be treated in an appropriate fashion.
5. My major desire is to see sensitivity analyses conducted to identify parameters in APEX, and the inputs, that impact the results. Given the formulation of APEX, I would think that an application could be approximated as a linear model, which might be instructive.

They should do sensitivity analyses to the PRB, and the quadratic model coefficients, as well as running 2002, and possibly a meteorologically "typical" year for one or two cities.

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Review of "Ozone Population Exposure Analysis for Selected Urban Area"

This short report provides additional detail that was used in developing Chapter 4 of the OAQPS staff appear, specifically discussing the APEX model and its application to the 12 urban areas. As noted above, APEX appears to be a technically appropriate and feasible model to estimate both current and modified exposures. It does suffer from a lack of discussion on model evaluation in this, and historical applications, and quantitative uncertainty analysis.

Page 4: 5th bullet: Are the 40% of the study of national scope statistically equivalent to the entire data set? If not, how and why not? What are the implications?

Page 5, point 2: How many individuals are needed to get stable results? They end up using 35,000, which seems like a huge number.

Page 11: Might there be a correlation between various residential variables (e.g., those with home and automotive air conditioners)? How is this captured in the model?

Section 2.4.3 "Mass Balance Model" is poorly presented mathematically. Looking at eq. 2-5, the del operator, "$\Delta$," does not have units, though here they use it as having units of $t^{-1}$. This is the case throughout the section, and ends up causing some problems. In the discussion of eq. 2-6, they say $dC_{out}(t)$ has units of ppm/hour, which as used is not the case. How they use $c_{in}$, $c_{out}$, etc., needs to be cleaned up.

Page 17, Last paragraph: it should be $dc_{in}/dt$.

Page 18: Wrong equations are referenced: (Equations 2-14, 2-15, and 2-16)

Page 22, 3rd paragraph: What is a stable #? Does it really have to be so big?

3.2.2: This section is unclear (and missing a ")")

Page 24, last sentence: "… differentiate BETWEEN people…"

Page 34: 4th paragraph "outdoor-other" (i.e., replace the comma with a hyphen.)

The major needs in this report are correcting the mathematical presentation of the mass balance model, presentation of historical and current model evaluation, use of a PRB distribution for each city (where they have included the anticorrelation between PRB and maximum ozone) and an uncertainty analysis. It could also do with some additional editing.

Review of the Rizzo memo:

This memo is an important supporting document to the "Ozone Population Exposure Analysis for Selected Urban Area" paper. As such, it should be quite clear as to what is done and why. At present, it is not. The explanations of the equations presented are difficult to understand, and it is not consistent in its use of subscripts. It should discuss the equation as a whole, with particular emphasis on the endpoints. The graphs provided are not at all well explained such that the various behaviors exhibited make sense. Some variables "loose" their subscripts, others it is not apparent how a single one-hour concentration that can be used for multiple 8-hr averaging periods gets rolled back. Also, how do they actually use the information in Table I? It is not well explained. Where do they use $S_i$? An example would help. This example should include a graph as to how the concentrations are adjusted, e.g., $C_j$' vs. $C_j$.

There is a "Data" section where they introduce a value S that appears to be different than used in the quadratic approach, which again has a subscript at times, and they use i as the index for year, where above it was used for the hour. This should be fixed.

Table II is a figure, and indeed, the only figure. The caption is insufficient to understand what they are portraying, and the explanation in the text is insufficient as well.

Also, I am not sure why there are kinks in the linear approach, and the memo appears to suggest that the author is uncertain as well. If these methods are being used, they should be understood by readers trying to delve in to the method.

# Dr. Elizabeth A. (Lianne) Sheppard

Lianne Sheppard
Risk Assessment Chapter 4, Staff paper Chapter 5
December 2005

*Chapter 4 of the Risk Assessment*

*Overall*

The first question to ask is a philosophical one: How should health effect estimates from time series studies be used in a risk assessment? The preponderance of evidence from all different types of studies suggests there is an ozone effect. The time series study models are valuable in part because they include exposures (concentrations) below the standards and thus are not subject to extrapolation. However, at this time I don't think there is good understanding of how closely the risks estimated in these studies relate to toxicity of $O_3$. The risk assessment estimates satisfy the criterion "… of a likely causal relationship between $O_3$ and the effect category." (p 4-7) The time series study estimates are more likely to be valid for testing the hypothesis of an association between $O_3$ and health than for estimation of the magnitude of the effect. I think more research is needed to fully understand whether time series study estimates are "causal".

It is important to note that these risk assessment estimates are restricted to short-term acute effects.

Model: I was confused by the different specifications of $\Delta y$ in (4-3) and (4-4). Why is one equation specified as the negative of the other? Why is there no distinction in the notation $\Delta y$? (After discussion at the meeting, moving this clarification, included for historical reasons, to an appendix will allow the clarification without introducing confusion for those unfamiliar with the history.)

There is no mention of how distributed lag coefficients are incorporated into the risk assessment. Since these are the sum of coefficients over multiple days, it should be noted how this is treated in the risk assessment. This can be done in an appendix section. All the equations given in the chapter implicitly assume there is a single exposure and health effect parameter of interest. This works fine for the single day lag models, but more detail is needed to explain how it is handled for the distributed lag models.

*Specific comments*

p. 4-6: When a single monitor has a missing observation, how is the monitor average created? Is there any adjustment for the long-term average for that monitor?

P 4-13: The discussion of interpretation of the single vs. distributed day lag models should reflect that these are different models that create different summaries of the underlying model for

the effect of exposure on health. When the underlying relationship has distributed effects, the distributed lag model is a more complete summary of those effects. It is not a very realistic summary because it is based in a one increment change for all exposures included in the distributed lag model.

p. 4-22: On p. 4-5 baseline incidence is defined as $y_0$ not y.

p. 4-28: The uncertainty due to using baseline incidence information is also more uncertain because there are no times when $O_3$ is absent.

P 4-32: The other reason thresholds are not discerned is the time series design. A time series study, due to its aggregate nature, is not well suited to estimating a threshold function that varies across different subgroups of the population.

4-32: I don't agree that we have a higher level of confidence in time series studies than ever before, particularly for the $O_3$ exposure. Refer to committee comments about chapter 7 of the AQCD.

P 4-37: The technical problem of counting the correct number of admissions from hospital discharge data should be readily overcome by expanding the time period in the initial discharge data extraction to dates well before and after the time period of interest, and then using inclusion/exclusion criteria based on admission date.

p. 4-38, beginning of 4.1.9.3.2. The first sentence implies that $\beta$ varies as well as the concentration data. Is this what was meant? I don't understand the argument in this paragraph.

P 4-39, end of 4.2 The point is that the estimates are consistent with a true effect or none. At least this source of uncertainty can be quantified.

*Chapter 5, Staff Paper*

p. 5-4 l.25-6: A key point that needs emphasis is that the risk assessment is limited to short-term effects. Most likely there are chronic effects that aren't included at all in the risk assessment.

p. 5-28 l 24-27: I don't think spatial variation of $O_3$ will have much impact on time series study estimates unless this spatial variation is also spatio-temporal (i.e. a change in relative amplitude not just location of the pattern).

p. 5-28 ll 29-31: While the risk estimates may be biased towards the null, the relative comparisons will not be affected when the bias is merely rescaling.

*Environmental Exposure Assessment*

p. S3: Define $\mu=a/(a+b)$ clearly.

# Dr. Frank Speizer

Comments on Ozone Health Risk Assessment for Selected Urban Areas: Draft Report, October 2005—Chapter 4
Submitted by: Frank E. Speizer

General Comment: The logic of this presentation is well presented but from my perspective was easier to read for the epi after reading the clinical studies. The problem will be that to do a series of potential different standards the issue will become confusing simply by the mass of numbers. Unless a method is presented that would allow for a graphic view of multiple standards in the same graph it will be hard to grasp the value of each change. Suggest use similar graphs that were used in the PM document.

Specific Comments:

Page 4-36, end of section 4.1.9.2.3

Why not consider doing highest and lowest for each city within the 3-year period rather than 2004 vs. 2002, and then compare to current standard and proposed reduction of standard?

Page 4.42, Figure 4.3. Need to make clear in label that in multi-pollutant models that each value represents O3 + one? other pollutant rather than addition of other pollutants sequentially (if that is the case).

Page 4.50 Text referring to Figure 4.3 also needs to clarify along same lines in the discussion of multi-pollutant models.

Table 4.9 Only 3 of 12sites significant in the single city models, but all significant in multi-city models. This needs to be expressed and discussed in text more explicitly.

Table **3.6 & 3.10 and 4.9 & 4.12 Using** the multi-city models in each of these tables one can estimate the deltas between "As is" and "current" suggests the impact that can be anticipated as related to actually levels seen. This suggests that there are differences gained in each sight that related to background levels. I wonder whether there may be a better way to express this than by simply presenting the 4 separate tables. For example, for the epi data in table 4.12 the range in improvement estimate is about 3 fold with the largest change in the highest sight (Los Angeles) and the lowest in several other sites. In contrast for data in the clinical studies the a 6-7 fold range of differences in improvement with what looks more like a baseline effect with those sites with the highest background levels having the greatest improvements.

Comments on Ozone Staff Paper, Chapter 5
Submitted by Frank Speizer

General Comments (specific questions raised by Staff)
*1. Technically sound, appropriately balanced, and clearly communicated?*

Although the presentation seems appropriate, there are a number of places that the data seem incomplete (see below). In addition, there seems to be what is probably a technical reason (because the data are simply not available) that is masked in an argument that what data are available would not be representative, when in fact the data, if there were available might in fact be more informative of a high risk group.

*2. health endpoints and c-r and e-r appropriate?*

Yes, except it might be worth looking also at 10% declines rather than just 15 and 20. Population declines in FEV of 10% are very large, even if often non significant for an individual. However, as median numbers there must be some individual who are put at significant risk at these levels.

*3. Methods for risk assessment.*

Better for others with more expertise to comment

4-6 not dealt with as technical document not yet reviewed.

Specific Comments:

Page 5-5 and page 5-6: Issue of not including respiratory symptom in healthy children and fact that restricted data on asthmatics raising difficulties for making quantitative estimates. Although I see the dilemma proposed I do not believe this should result in these estimates being left out. I will reserve judgment at this point as I read through the rest of the chapter, but the fact that some of the recent studies do not agree with the previous work does not mean the previous data were wrong, and therefore the sum total of all the data need to be considered. The same is true for the asthma data. Clearly inner city may be at higher risk, but an estimate of risk in this group **using their data alone** would still appear to be warranted as it provides no margin of safety for this group and maybe a certainly level of safety for a population with more advantages.
Ditto top of page 5-7 that excludes increased respiratory symptoms among inner city asthmatics. Having this information for a high risk group certainly would set the bounds for the "urban population" and that in it would be useful.

Page 5-23 para 5.3.2.4 and Table 5.2. Although the text suggests that population sizes and various age groups are being assessed, the table belies the statement. It is not clear why the details are not in the table. Certainly they are available (if not for ages greater than 30 certainly for 15-65 and 65+.) Also not clear why table 5.3 is incomplete.

Page 5-26, Table 5.4. It is disappointing that there are no overlap statistics for any of the cities. It would be nice to see a range of values of admissions for any of the major diseases indicated to

see how different (or the same) they are across the cities (since the risks are to be applied nationally).

Page 5-28, line 32-33. This important statement will need to come up again as we get to interpretation of risk assessment. It suggest that an adequate margin of safety is being ignored we one uses the actual risk assessment value calculated from these data.

Table 5.5 and Table 5.6: I am having trouble discerning the difference between these two tables other than the effect estimates are about 10 lower in 5.6 than in 5.5. Is there a labeling problem?

The text needs to be expanded to include additional data on alternative standards and key observations. Given that the chapter is incomplete consideration should be given to getting rid of some of the redundancy in the tables and figures. Not all are needed to be presented.

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Comments on Ozone Staff Paper, Chapter 6
Submitted by Frank Speizer

General Comments:
Through page 6.14 an excellent summary of the preceding chapter and tables. Few minor points in wording are indicated below. The discussion of the Indicator (Section 6.3.2), Averaging time (Section 6.3.3.) and Form (Section 6.3.4) are appropriate and adequate. The discussion of Level (section 6.3.5) raises interesting questions and supports the proposed staff work to construct estimates down to levels of .06ppm. This will represent considerable additional work and rather than do it for 3-5 highest over 3 years suggest it be limited to 3 for .08ppm and 4 for .07 and .06ppm.

Specific Comments

Page 6-9, para beginning line 14. Last sentence beginning on line 28: It is not clear how this matches up with table 5.5, and carried over to table 6.2, which I believe suggest that the median number children with at least one event of a 15% drop in FEV is about 10%. This does not strike me as “rare for individuals”

Page 6-13.line 20. I think there are a number of people who would take issue with the description that would appear to minimize the adverse consequences of transient drops of 15-20% in FEV. Suggests rephrase. In addition although the overall average is 7 events per season it is likely that there are only a small fraction of people experiencing these events and therefore among them they will be having a lot more events. Thus, the average number becomes meaningless in considering margin of safety for the venerable group.

# Dr. James Ultman

**Review of OAQPS Staff Paper – First Draft**
James Ultman

Chapters 3 and 5.

The only general comments I have regard the strengthening of subsections 3.7.1 and 5.2.1.3 with regard to probabilistic exposure-response functions.

1) In section 3.7.1, probabilistic exposure-response functions should be carefully defined as illustrated with a graph such as figure 8-2 from the CD.
2) In section 3.7.1, probabilistic exposure-response functions should be compared to mean exposure-response functions.
3) In section 3.7.1, the need to include intersubject variability using the probabilistic approach should be stressed. Even when a mean exposure-response function utilizes multiple measurable factors (such as exposure concentration, ventilation rate, age and exposure time), there is still a large unexplained intersubject variability (e.g., McDonnell et al. Am. J. Respir. Crit. Care Med. 156:715-722, 1997). The probabilistic approach does not suffer from this problem.
4) I think that section 5.3.1.3 on the manipulation of the probabilistic exposure-response functions could benefit from a graph showing the final probabilistic boundary that was actually used.

| Page | Line | Specific Comments |
|---|---|---|
| 3-5 | 10-11 | Change statement to "…in the epithelial lining fluid (ELF) and the epithelial cell layer, and is not absorbed…" |
| 3-4 | 17 | What happened to chapter 4? |
| 3-8 | 32 | Delete "including" |
| 3-8 | 34 | Delete "morphological effects," |
| 3-10 | 20 | Change wording to "…equivalent inhaled $O_3$ doses…" |
| 3-10 | 17-21 | This is an important point that is not adequately supported by the current presentation on page 6-8 of the second draft of the CD. |
| 3-16 | 22 | Change wording to "…because the epithelium in this region…" |
| 3-17 | 3-5 | It is not clear what "susceptibility factors" means. Ozone-induced tissue damage depends on the delivered dose of ozone and its toxic reaction products as well as the biological sensitivity of the tissue. So, what does it really mean to say that ferrets and monkeys have similar responses and rats have lesser injury. Are they being compared at comparable delivered doses, exposure concentrations or what? |

# Dr. Sverre Vedal

**December 2005**
**Critique of 2nd Ozone Staff Paper draft**
**Sverre Vedal**

**Chapter 3 (Health effects)**

Bigger points.

1. In general, this chapter takes a well-balanced approach to summarizing and integrating the available health evidence. There are some exceptions. For example, although there is a good interpretation of the effects on cardiovascular hospitalizations, the Ch.7 CD conclusion regarding warm season effects, which is an overstatement based on the appropriate figure in the CD, is brought forward here (p.25 and 48). The conclusions and summaries are generally good: chronic effects (p.21,23); measurement error (p.33); temporality (p.37); single vs, multi-day lags (p.38).
2. Defining adversity based on level of lung function is complicated in the context of ozone because it is not clear that the acute decrease in inspiratory capacity (hence the major determinant of the decline in FVC and FEV1) is not beneficial in preventing more marked exposure. A similar argument can be made for irritant symptoms. The Staff Paper is similarly confused (justifiably) on this point (p.54. line 31) when it is suggested that relative lack of symptoms and lung function response in children and the elderly may place them at greater risk. It is difficult to have it both ways (adverse and beneficial), unless qualifiers are added. This issue needs to be dealt with in order, at the very least, to avoid confusion.

Smaller or detailed points.

Page

3. Bronchoconstriction (here and p.41) is identified as the lung function effect, when in fact this is relatively minor compared to reduced IC and its effects on FVC and FEV1. Also, on p.4, in the discussion of lung function, where is IC and its major role in affecting FVC and FEV1?
21. As was concluded in discussions on the CD, reference to the Calderon study on chest x-ray findings should be deleted.
23. The Plopper reference (1998) here is not correct; this is a reference to work in adult monkeys, not infants, and is not about airway remodeling.
23. (& p.68 especially). The Sherwin pathology findings are given a prominent airing; as for the Calderone study, this should probably not be emphasized, or possibly even excluded from the discussion.
23. Note that there were only 20 high-exercising children with new asthma in the high ozone area vs. 9 in the low ozone area.
24. Note that the Peters 2-hr effect was not seen in her latest study this year (HEI report); also relevant to p.38.
25. As in the CD, it is a stretch to use widening of the A-a gradient and V/Q mismatch to argue for cardiovascular effects.
25. line 12. Effects on arrhythmias are brought up, but no mention is made that these are based on implantable cardioverter studies (Dockery/Rich), not HRV studies.

29. It is some oversight to not also bring up that for some specifications of ozone exposure in ACS 2002, there was an ozone effect in the warm quarter, as there was in Krewski 2000 (HEI Report p.174); should also add to p.30.
30. To be more precise on AHSMOG, there was an effect for lung Ca, but not for total mortality.
31. I would question the conclusion that there is "strong" evidence on mortality and ozone, as expressed in my concerns on Ch. 8 CD.
32. Interpreting the epidemiological associations as strong is wrong. The 2004 Surgeon General report on smoking does define strength to be a function of size and precision (statistical significance) of the effect estimates. However, associations cannot be strong if effects are small, but precise, which is usually the case here, especially in multi-city studies.
34. Is the correlation between aggregate personal concentrations and ambient concentrations adequate to be comfortable in the use of ambient concentrations in time series studies in the absence of correlation with individual personal concentrations? (line 16) Yes, use of c-r functions essentially incorporate population exposure issues, but justifying use of central monitors because they are associated with aggregate personal exposures may not be valid.
42. (and Table 3.1). Like recommendations for Ch.8 for human cardiac effects, more relevant information from Gong 1998 on heart rate and cardiac work should be included in this table rather than indirect effects on the A-a gradient or V/Q.
44. One cannot use the Mortimer 2002 findings to conclude that asthmatic children are a particularly susceptible since the study was restricted to them and did not compare their effects to those in other groups.
48. line 21. In fact, one study shows a negative association of ozone and mortality (p.7-92), so to be absolutely correct, not all are positive, as opposed to what is stated.
50. line 4. I would add here (and p.58) that there is little evidence for long-term effects on lung function, especially given Gauderman 2004.

**Chapter 4: Exposure**

Page

4. Ozone exposure studies are described as having been done, but what is the bottom line?

Should we use models given the personal monitoring data? Could do if have APEX estimate 24-hour exposures.

I don't quite understand why exposure is not estimated for the population reflected in time series mortality studies (i.e., the unwell elderly). It is clear that exposure estimates are needed when the risk assessment is based on experimental studies. I guess this doesn't matter when risk estimates are based on observational studies, since the c-r functions from these studies obviate the need for exposure estimates.

**Chapter 5: Risk assessment**

Page

6. The selection of mortality as a major endpoint in the risk assessment is ill-founded at this time for several reasons:

i. Total mortality is driven by cardiovascular mortality. The lack of evidence for effects on cardiovascular hospitalizations detracts from the coherence of ozone effects on cardiac mortality.

ii. The evidence relies on time series studies which in this setting (the ozone setting) can be questioned for several reasons: First, the time series studies as a group indicate that all of the criteria pollutants are associated with mortality. Therefore, they do not allow solid conclusions

regarding individual pollutants. Second, a strong case has been made that in many instances, there is no correlation between personal exposure to ozone and concentrations at central monitors. Third, the population affected in the mortality time series studies has exposures to ozone that are at the low end of the distribution of ozone exposures.
I have therefore have serious reservations about including total and cardiovascular mortality in the risk assessment. I would recommend limiting the risk assessment to respiratory outcomes. A better case can be made here for including respiratory mortality, even though findings are based on time series studies, since the supporting evidence for the less adverse respiratory outcomes (including respiratory ER visits) is much stronger than for cardiac outcomes.

28. The evidence for no threshold down to background concentrations is based on time series studies, particularly the mortality studies. The role of measurement error in blurring thresholds that may exist is much more relevant to ozone time series studies than for PM studies.
41. Use of a distributed lag effect estimate for the c-r function is problematic.

General points:
1. A continued concern is the persistent use of a non-integrated, non-probabilistic risk assessment, which today seems inadequate.
2. Several large sources of uncertainty (e.g., model specification, exposure, etc.) are not incorporated into the sensitivity analyses, and are certainly not reflected in the 95% CI's of the concentration-response functions.

**Chapter 6 (primary NAAQS)**

Bigger**:**
Page
6. line 16. Is the evidence good that asthmatics have larger lung function declines with ozone?
7. line 15. I think describing the findings regarding respiratory ER visits as "inconclusive" is too strong.
8. line 8. Findings regarding cardiovascular hospitalizations, on the other hand, are inconclusive, even in the warm season.
8. line 32. Arguments for the causal association for mortality are suspect.
16. The Peters findings of very short term effects on myocardial infarction have not been seen in her larger, more definitive, study (HEI 2005).
19. line 4. "Inconclusive" seems inconsistent with much of the CD and SP wording.
19. Para 2. Again (as in Ch.5), no threshold argument is based on time series studies.
20. Level of 0.06 ppm is pretty arbitrary, from a science perspective. The fact that Bell 2004 showed associations that persisted when data were restricted to days of less than 0.06 ppb will cause some confusion. This is less relevant if time series mortality studies are not considered in the risk assessment. Why 60 ppb vs. 70 vs. another value? It seems quite arbitrary, so better motivation is needed.

Smaller:
17. Line 5. There is again reference to the Sherwin study.

# Dr. James Zidek

**Revised Comments of the Staff Report 1st Draft**
**James V Zidek, December, 2005**

## CHARGE QUESTIONS

My detailed comments respond to a number of the issues raised below and only summaries are provided here.

### O3 AIR QUALITY INFORMATION AND ANALYSES (CHAPTER 2):

1. To what extent are the air quality characterizations and analyses clearly communicated, appropriately characterized, and relevant to the review of the primary and secondary O3 NAAQS?

**The results are generally clear and very well communicated. In particular, the Report provides a good characterization of the concentration field of the current criteria metrics. However some improvements are needed and these are included in my detailed comments.**

2. To what extent are the properties of ambient O3 appropriately characterized, including policy-relevant background, spatial and temporal patterns, and relationships between ambient O3 and human exposure?

**Some indication is needed of the level of uncertainty associated with the estimates of the PRB field. In particular, evidence I have seen suggests that at least short-term temporal aggregates of CTM outputs overestimate measured concentrations. The relationship between ambient and personal exposures is very well discussed in qualitative terms. In general, very little is known in quantitative terms between these two especially at the hourly levels.**

### O3-RELATED HEALTH EFFECTS (CHAPTER 3):

2. What are the views of the Panel on the appropriateness of staff's discussion and conclusions on key issues related to quantitative interpretation of the epidemiologic study results, including, for example, exposure error, the influence of alternative model specification, potential confounding by co-pollutants, and lag structure?

**The AQCD (2nd Draft) and the Report (1st Draft) address issues I raised in my comments about the AQCD (1st Draft). The discussion of exposure error and its effects is generally very good. Some improvements are suggested in my detailed comments.**

**EXPOSURE ANALYSIS (CHAPTER 4 OF THE DRAFT O3 STAFF PAPER AND DRAFT EXPOSURE ANALYSIS TECHNICAL SUPPORT DOCUMENT):**

1. To what extent is the assessment, interpretation, and presentation of the initial results of the exposure analysis in Chapter 4 technically sound, appropriately balanced, and clearly communicated?

**Overall, the results seem technically sound and the reports, well written.**

2. Are the methods used to conduct the exposure analysis technically sound? Does the Panel have any comments on the methods used?

**Methods like those proposed are the only ones available for scenario analysis, a vital part of any hypothetical criteria changes. APEX is the most advanced of any of those with which I am familiar and seems very appropriate since it is used in conjunction with chamber study estimates of concentration-response risk estimates for risk analysis.**

4. To what extent are the uncertainties associated with the exposure analysis clearly and appropriately characterized in both Chapter 4 and the draft Exposure Analysis technical support document?

**On the whole, these reports have done well to explain those uncertainties. However, the implications of those uncertainties are unclear, especially in relation to the 95% prediction intervals for scenario benefits.**

5. What are the views of the Panel on sensitivity analyses that should be conducted to evaluate the influence of uncertainties in the exposure analysis?

**For pNEM at least the sensitivities to the choice of model parameters have been investigated and presumably the same sensitivities obtain in APEX. I would note however that APEX's model parameters are random with distributions estimated from data. The uncertainty in these estImates does not seem to have been propagated through to the risk assessment and here is where sensitivity does become an issue, particularly with respect to the estimated distribution of air exchange rates, a principle determinant of indoor exposures.**

**An assessment of the accuracy of APEX exposure forecasts would be desirable to convince the community that the model really does work.**

**Replacing population counts with population fractions and running APEX repeatedly would yield predictive exposure distribution estimates for use with those CRFs to generate estimates of expected excess morbidity and mortality due to exposure.**

## DETAILED COMMENTS

### Chapter 2:

2-13 The informative plot on this page (and the one on the following page) does not seem to be in the AQCD 2nd Draft. It addresses a concern I raised in my comments on AQCD 1st Draft about the spatial coherence of the field of extremes calculated over a large time domain of values. It seems to suggest that the field is quite flat.

However aggregating data as in this county plot may disguise some important details. Firstly this seems to be a plot of 3-year averages of the 4th largest value. (The caption should say so.) Individual plots by year would have shown the stability of this map over time. Indeed, the cynical might see this as an attempt to conceal the true complexity of that field of extremes. Since that field is a continuum, a contour map of the field [with an associated standard deviation map showing the reliability of those contours] would have more natural. Moreover, it would show some of the fine detail, for example, in those big flat patches over California. Finally, it would have avoided the artificial discontinuities at county boundaries.

An analysis like the one I presented in my AQCD 1st Draft comments would be desirable for selected sites in some of the high pollution areas. It would help address an issue that always arises in the study of extremes like the annual maximum, 4th annual maximum and so on. In particular, it would shown the directions in which these fields hang together as the time-span of the calculated extremes increases from daily to weekly to monthly maxima. This kind of analysis will indicate how thoroughly the criteria metrics cover the populations they are meant to protect. Based on my earlier analysis, I conjecture that at least some areas that would not well covered by metrics of the current type.

2-20 What is the range of the boxes in the plot? The caption should state it in this and later figures for clarity.

A useful addition here would be a more detailed analysis, showing the fraction of sites with metric values above specified thresholds such as 70, 80, 90ppb, etc. The major urban areas with site-metric values higher than these thresholds would also be informative. The same comments pertain to Figure 2-10. Are there any “gaps” over

which the threshold could be moved without changing the number of sites with metric-levels above threshold?

2-25 Here again the captions need work as in the succeeding box plots.

2-29 line 5: Change “is” to “are.”

2-36 line 32: How reliable are the CTM-based estimates? I assume the range stated in this line reflects simulated data (model) variation over days, not the range to be used for any one day. If so, this should be so stipulated to avoid risk of misinterpretation. In any case, work I have seen shows MAQSIP and CMAP at least to be upwardly biased especially during the afternoon. Is GEOS-CHEM unbiased? Was the model run for any year other than 2001 and if not why not? How much variability from year-to-year would be seen?

Quite a number of relevant comments can be found in my comments on the AQCD 1st and 2nd drafts. Briefly, the deterministic and statistical modeling cultures are very different. In the latter models are regarded as just that and not ``reality'' in any sense, hence the emphasis, from the time of Gauss at least, on characterizing their uncertainty [although the machinery for addressing model uncertainty properly has only been available in recent years].

2-41 **line 14:** I am not sure what this sentence is meant to say. Are “observations” different from “observational results” as the sentence suggests? What does “prior modeling” mean? (In statistics, it means modeling the prior distribution, but obviously that cannot be what is intended here.) What is meant by the “range of PRB estimates” and how does the range of 25-45 ppbv relate to the range given on page 2-36 of 15 – 35 ppb? Can a common scale be used to make these comparable?

**line 24:** This does not seem to be a sentence.

**CHAPTER 3**

The chapter touches on the important association between temperature and ozone, but does state clearly that the relative risk RRs being used were adjusted for meteorology as suggested in the AQCD Draft.

3-34 **line 10:** I did not understand Staff reaction to my question on this line during the CASAC Consultation meeting. Reflecting on their answer, I think what they were making the counterfactual argument that ozone could be reduced while holding everything else constant. That would ensure the applicability of the relative risks estimated through observational studies to reduced ozone fields as well. If that was the argument, then that assumption should be explicitly stated, recognizing at the same time that it is not very plausible. In any case, some clarification on that point seems necessary.

3-62 **line 36**: “Tables 3.2 or 3.3 above”

**CHAPTER 4**

4-1 **line 21**: A space is needed just before "levels"

4-6 APEX is a valuable tool for exposure assessment as well as predicting the benefits of a pollution abatement program. In particular, it can answer "what if" questions under roll back scenarios.

Like the CTM models used in calculating the PRB, APEX is only a model and not "reality. Therefore the more testing that can be done the better, especially since this methodology seems likely to be used in lots of other future applications. I am fairly confident that APEX, viewed as generating a predictive distribution rather than mere point estimates, will be fairly well calibrated (at least at the daily level). By this I mean that the 95% prediction interval would contain actual exposures about 95% of the time. That in turn would mean uncertainty in the point estimates has been appropriately characterized so that measurement error could be properly accounted for in the risk assessment. [I will say how more specifically below.] That confidence derives from a small-scale assessment I did with my research collaborators (and discussed in my comments on AQCD Draft #1) on an APEX-like model, albeit for PM2.5, an encouraging result. Of course, a fuller assessment of APEX predictions for ozone exposures would obviously be desirable.

4-7 **line 23**: The randomness of model parameters needs some explanation in the Report. Their distributions could be interpreted by readers as Bayesian priors, reflecting (epistemic) model uncertainty, albeit with an empirical Bayes twist. In that interpretation, variability of the predictive output distribution would reflect that epistemic uncertainty as it propagates through the model, rather than only process (aleatory) uncertainty. It might be worth stating that these parameters are actually random effects so that variability in the predictive distribution represents aleatory uncertainty. Of course, that then pushes the issue of model uncertainty to a higher level on that staircase of infinite regress that Mosteller and Tukey famously referred to. (See my comments below re Table 5.5.)

4-12 **line 8:** Interpreting counts is difficult, in particular person-hours and that led to some consternation at Dec CASAC meeting. I think a different approach should be taken, that would characterize APEX outputs as a predictive distribution of personal exposure. Results could be then be characterized in a much more intuitive way in terms of a typical population member's exposure. For example: "The chances are 93% that a typical child's exposure would exceed 85ppb that day." As well this characterization of APEX output would have an operational value in terms in risk assessment. I have attached a supplement indicating how all this could be done.

**CHAPTER 5**

**Table 5.5** The estimated 95% intervals seem to be just those in the relative risk estimates propagated through the linear concentration-response function to the personal exposure outputs. I did not find the discussion of this calculation in the technical paper, but presume APEX ozone exposure outputs were generated and pumped through the FEV concentration-response function to get their effects on the FEV. The fraction of these exceeding a specified level such as 15% were then calculated and reported in the Table. Similar calculations were done, first for the lower 95% limit for the effects coefficient and then for the upper, to get the 95% interval.

However, the APEX estimates are themselves subject to sampling uncertainties. No indication is given of their size and whether these have been incorporated in the 95% intervals. Additional uncertainties derive from the data-based estimates of parameter model distributions but these do not seem to have incorporated in those intervals. [That calculation might actually be feasible using a bootstrap approach if APEX runs sufficiently fast, say by restricting analysis to one or two selected sub-populations.] However, model uncertainty is a major source of uncertainty that is difficult to calculate. That should at least be acknowledged with respect to the quantities presented in tables like this one.

# Supplementary Material: APEX as a predictive distribution

Suppose $g$ designates a population subgroup, $g = 1, \ldots, G$ with a fraction $p_g$ of the total population of interest, for example, children, aged $6 - 12$ years. Suppose for example, we wish to estimate $\mu_g$, the ***expected*** number of daily exceedances of $c \equiv 0.70ppm$ for a typical (randomly selected) child in group $g$. Let the corresponding number for a particular randomly selected child be $N_g$ so that $\mu_g = E[N_g]$, the group $g$ average value of that number. In other words "E[]" in this expression represents the ensemble average.

We obtain a useful representation the required expected value by first letting $T_{gt}$ denote the hourly maximum for day $t$ and then

$$I_{gt} = \begin{cases} 1 & T_{gt} > c \\ 0 & T_{gt} \leq c. \end{cases}$$

In other words, $I_{gt}$ is an exceedance marker for group $g$ on day $t$. It counts a "1" if an exceedance occurs that day. Finally we have

$$N_{(g)} \equiv I_{g1} + \ldots + I_{gT}$$

and

$$\begin{aligned} \mu_g &\equiv E[N_{(g)}] \\ &= E[I_{g1} + \ldots + I_{gT}] \\ &= E[I_{g1}] + \ldots + E[I_{gT}] \\ &= P(T_{g1} > c) + \ldots + P(T_{gT} > c). \end{aligned}$$

In a similar way the variance of $N_g$ may be found only this would not involve the pairwise joint probabilities $P(T_{gt} > c, T_{gt'} > c)$ for all day pairs, $t$ and $t'$. Presumably this would be zero if those days are widely separated, but then that would depend on the autocorrelation in the exposure sequence.

To estimate the unknown $\mu_g$, run APEX repeatedly to generate exposure sequences for randomly selected (composite) members of that group. Aggregate the successive exposures to get at the hourly the exposure sequence, starting at day 1, hour 1 and ending at day $T$:

$$X^{(r)}_{g11}, \ldots, X^{(r)}_{g1,24}, X^{(r)}_{g2,1}, \ldots, X^{(r)}_{gT1}, \ldots, X^{(r)}_{gT,24}$$

for run $r = 1, \ldots, R$. Then find the sequence of daily maxima:

$$\begin{aligned} T^{(r)}_{g1} &= \max_{j=1}^{24} X^{(r)}{}_{g1j} \\ &\vdots \\ T^{(r)}_{gT} &= \max_{j=1}^{24} X^{(r)}{}_{gTj}. \end{aligned}$$

Finally estimate $\mu_g$ by finding for each day, $t$, the fraction of the runs for which $\{T^{(r)}_{gtl} > c\}$. That fraction estimates $P(T_{gT} > c)$. Adding these estimates up over days yields the required estimate of the expected number of days a typical child would be exposed.

To get population level estimates of $\mu$, the expected number of days a typical person's maximum daily exposure exceeds $c$ would require the formula $\mu = \sum_{i=1}^{G} p_g \mu_g$. That quantity could be estimated in the obvious way.

More general calculations can be made by estimating APEX's predictive distributions, say for $M_{gt}$, for example, based on the repeated runs. Let $\hat{f}_{M_{gt}}$ denote the estimate of the distribution for the maximum on day $t$. That estimate could be as simple as a histogram. Then if

$$K_g \frac{\exp[RR_g M_{gt}]}{1 + \exp[RR_g M_{gt}]}$$

were the concentration response function for day, for an appropriate constant $K_g$, the residual expected health outcome for that day would be

$$\int K_g \frac{[\exp RR_g x[}{1 + \exp[RR_g x]} \hat{f}_{M_{gt}}(x) dx,$$

a quantity that might need to be calculated numerically. The population impact could be found by summing these impacts over days and then averaging over groups.

# Dr. Barbara Zielinska

## Comments on the 1st Draft Staff Paper
## Chapter 2

**Barbara Zielinska**
**DRI**

My responses to the charge questions from Dr. Martin memo (November 14, 2005), regarding Chapter 2, are as follows:

1. *To what extend are the air quality characterizations and analyses clearly communicated, appropriately characterized and relevant to the review of the primary and secondary $O_3$ NAAQS?*

In my opinion, this chapter of the 1st Draft Staff Paper is well written and presents a concise summary of the information contained in Chapter 2 and 3 of the 2nd draft CD. However, the chapter needs more work, as several important issues were left out or inadequately characterized, as discussed below.

2. *To what extend are the properties of ambient $O_3$ appropriately characterized, including policy relevant background, spatial and temporal patterns and relationships between ambient $O_3$ and human exposures?*

Although Section 2.2, that covers chemical and physical properties, formation and transport of ozone, mentions "other oxidants", it does not include any information regarding this topic. It would be important to summarize briefly the discussion in Chapter 2 regarding other photochemical oxidants and the role of ozone in the atmospheric transformation processes that may results in the formation of more toxic gas- and particle-phase products.

The ambient $O_3$ levels, its temporal and spatial variability, long-term trends, and characterization of ozone episodes, seem to be adequately summarized in this chapter. However, there is no information regarding relationships between ambient $O_3$ and human exposures. The modeling of human exposure to ozone is discussed in Chapter 4 of the Staff Paper; however, there is no information in both chapters how the actual personal human exposures compare to the ambient central monitoring data.

The policy relevant background (PRB) issue is not very well characterized as well. The statement that PRB cannot be derived from measurements and must be based on modeling (page 2-36, lines 26-28) is somewhat controversial. As documented in Chapter 3 of the CD, there are still some uncertainties involved with atmospheric models and thus the predictions resulting from an ensemble of models should be compared with each other and with observations. To relay on one global atmospheric model only, seems to be a little limited approach. The statement on page 2-41, lines 14-17, is confusing – background estimates from observations are different from observational results and prior modeling? This doesn't make sense. The intended removal of most of the PRB relevant text (as Staff indicated during the CASAC meeting) is not going to fix

the problem – PRB is important in subsequent health risk estimates and has to be covered adequately in this chapter. I think this section needs more work.

3. *Does the information in Chapter 2 provide a sufficient air quality related basis for the human health and environmental effects and assessments presented in later chapters?*

I think that in overall Chapter 2 requires some more work, although it represents a very good start.

Minor Comments:

1. Figures 2-2 and 2-3 would be more informative if the data are not shown on the countywide basis, since there are appreciate data variations within counties.
2. Figure 2-3. For X = > 0.119, the population of 39 counties is only 40,569 people?
3. Section 2.5.2.2. Comparison of different ozone measurement matrices would be useful.
4. Page 2-27 – 2-28, Figures 2-14 and 2-15. What are the units of ozone concentrations?
5. Page 2-41, lines 24-26. What does this sentence mean?
6. Page 2-41. The reader is erroneously referred to Chapter 2 Annex (AX2) here, whereas Annex AX3 is meant.

## NOTICE

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