UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

December 3, 2009

EPA-CASAC-10-004

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

Subject: Consultation on EPA's *Draft Integrated Review Plan for the National Ambient Air Quality Standards for Particulate Matter*

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 — held a public advisory teleconference meeting on November 13, 2009. The purpose of the teleconference was to conduct a consultation with staff from the Agency's National Center for Environmental Assessment (NCEA) and EPA's Office of Air Quality Planning and Standards (OAQPS) on the Agency's *Integrated Review Plan for the Ozone National Ambient Air Quality Standards Review* (External Review Draft, September 2009). The Panel generally found the *Integrated Review Plan* to be a well-conceived roadmap for the upcoming Ozone National Ambient Air Quality Standards (NAAQS) review.

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 Enclosure A of this letter, and the CASAC Ozone Review Panel roster is found in Enclosure B.

Finally, some Ozone Review Panel members' individual written comments are provided in Enclosure C.

Sincerely,

/Signed/

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

Enclosures

Enclosure A

U.S. Environmental Protection Agency
Clean Air Scientific Advisory Committee (CASAC)

CHAIR

Dr. Jonathan M. Samet, Professor and Flora L. Thornton Chair, Department of Preventive Medicine, University of Southern California, Los Angeles, CA

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Dr. Donna Kenski, Data Analysis Director, Lake Michigan Air Directors Consortium, Rosemont, IL

Dr. Armistead (Ted) Russell, Professor, Department of Civil and Environmental Engineering, Georgia Institute of Technology, Atlanta, GA

Dr. Helen Suh, Associate Professor, Department of Environmental Health, School of Public Health, Harvard University, Boston, MA

Dr. Kathleen Weathers, Senior Scientist, Cary Institute of Ecosystem Studies, Millbrook, NY

Enclosure B

U.S. Environmental Protection Agency
Clean Air Scientific Advisory Committee
Ozone Review Panel

CHAIR

Dr. Jonathan M. Samet, Professor and Flora L. Thornton Chair, Department of Preventive Medicine, University of Southern California, Los Angeles, CA

MEMBERS

Prof. Ed Avol, Professor, Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA

Dr John Bailar, Scholar in Residence, The National Academies, Washington, DC

Dr. Michelle Bell, Associate Professor, School of Forestry and Environmental Studies, Yale University, New Haven, CT

Dr. Joseph Brain, Philip Drinker Professor of Environmental Physiology, Department of Environmental Health, Harvard School of Public Health, Harvard University, Boston, MA

Dr. David Chock, Retired, Environmental Modeling Group, Physical and Environmental Sciences Department, Research and Advanced Engineering, Ford Motor Company, Dearborn, MI

Dr. William Michael Foster, Professor, Pulmonary and Critical Care Medicine, Duke University Medical Center, Durham, NC

Dr. H. Christopher Frey, Professor, Department of Civil, Construction and Environmental Engineering, College of Engineering, North Carolina State University, Raleigh, NC

Dr. Judith Graham, Independent Consultant, Independent Consultant, Pittsboro, NC

Dr. David Grantz, Director, Botany and Plant Sciences and Air Pollution Research Center, Riverside Campus and Kearney Agricultural Center, University of California, Parlier, CA

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

Dr. Daniel Jacob, Professor, Atmospheric Sciences, School of Engineering and Applied Sciences, Harvard University, Cambridge, MA

Dr. Donna Kenski, Data Analysis Director, Lake Michigan Air Directors Consortium, Rosemont, IL

Dr. Steven Kleeberger, Professor and Lab Chief, Laboratory of Respiratory Biology, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC

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

Dr. Howard Neufeld, Professor, Dept. of Biology, Appalachian State University, Boone, NC

Dr. Armistead (Ted) Russell, Professor, Department of Civil and Environmental Engineering, Georgia Institute of Technology, Atlanta, GA

Dr. Helen Suh, Associate Professor, Department of Environmental Health, School of Public Health, Harvard University, 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, University of Washington, Seattle, WA

Dr. Peter Woodbury, Senior Research Associate, Department of Crop and Soil Sciences, College of Agriculture and Life Sciences, Cornell University, Ithaca, NY, U.S.A.

SCIENCE ADVISORY BOARD STAFF
Dr. Holly Stallworth, Science Advisory Board Staff Office, Washington, D.C.

Enclosure C

Compendium of Individual Comments

CASAC Ozone Review Panel

Integrated Review Plan for the Ozone National Ambient Air Quality Standards Review

(External Review Draft, September 2009)

Bell (Dr. Michelle Bell)

Overall, the document is very thoughtful, well-written, and clear. The following are some suggestions:

Please clarify the language regarding susceptible, vulnerable, and sensitive subpopulations. These terms are used in a variety of contexts in general, so their unique uses here should be stated explicitly, with examples. These concepts may be particularly confusing for the general public or others who do not work in fields where such terms are used in the manner in which EPA intends. The text should acknowledge whether, or in what cases, these terms are not mutually exclusive.

Establishing the policy relevant background (PRB) level [see page 39] is by no means trivial, and the draft Review Plan acknowledges some of these limitations. The Plan notes that greater emphasis will be placed on understanding the contribution of different components that contribute to PRB [see page 40]. However, given the complexities of establishing a PRB and the wide range of approaches available, it would be helpful to have more information on how the PRB will be determined and how sensitivity analyses might be conducted. As the document is a plan, not a detailed methods design, some general information may be appropriate, as opposed to specifics, although the current document could use more information.

The draft Review Plan acknowledges that the uncertainties involved in this evaluation will include both qualitative and quantitative factors. Qualitative uncertainties will be categorized by the approximate degree of uncertainty [see page 42]. This attention to various types of uncertainties is appreciated, as numerical estimates will not be possible for all uncertainties. The nature of how uncertainty will be addressed is unclear and could use more explanation. In particular, how uncertainty analyses will be conducted for concentration-response curves and threshold effects is vague. Even though not much detail is given on how uncertainties throughout the system will be addressed, it seems apparent from the Plan that much thought has been given to this issue. Given that the document is a plan, it may be appropriate to have general information rather than specifics. Analysis of uncertainties has been conducted by EPA for a variety of similar settings for other pollutants, such as particulate matter, so references to such documents may be a helpful way to briefly give some details on the overall planned approach.

Bailar (Dr. John Bailar)

Comments on "Integrated Review Plan for the Ozone National Ambient Air Quality Standards Review – External Review draft"

Overall, this draft is clear, concise, and nearly complete. I have only a few comments, none of which require major revisions. These are not in any particular order.

The draft needs a little technical editing. Also, there is some redundancy, which is a bit dangerous when things are not repeated in exactly in the same way because persons who want to bring down bigger things may exploit small differences.

There should be a little more on how variables will be selected for sensitivity testing. Also, there should be comment on how that testing will be done. In particular, will variables be tested for sensitivity only one by one, or will the testing examine combinations of variables simultaneously. This may matter if there are interactions or other relations among the variables selected for sensitivity testing.

There should be more on the relation between concentrations of O_3 at central testing locations and what people actually inhale in various circumstances (at heavy outside work, in a hospital bed, walking to school beside a busy highway, driving to work in a closed car, etc.).

Please expand the discussion of the quality of the monitor measurements.

There should be more stress on possible differences in biologic mechanisms between chronic and acute effects of O_3.

I believe that there is only a single, very brief reference to the difference between confounders and effect modifiers. This is a big issue and needs more exploration.

There has been a long history of under-regulation by EPA and other regulatory agencies in that standards often move down and never up. In short, future analysts are likely to have evidence that standards should have been tighter. EPA may be unable to regulate until pretty good evidence of an effect is in hand, but the likelihood of a need for change in the future should be mentioned.

There should be some comment on the difference between individual concentration-response relationships and population-wide relationships, which are necessarily much flatter in slope because they are averages of individual relationships.

Similarly, there should be some comment on estimating the effects of a change in regulatory standard on persons whose exposures is already below the new limit – Some of them will benefit for efforts to reduce O_3 in the higher exposure areas, and ignoring that will tend to underestimate the benefits of regulation.

Chock (Dr. David Chock)

Overall, the IRP was excellently prepared. I only have a few brief comments to make.

Ch. 3. General comments: In considering the ozone NAAQS, it is important to understand the role of co-pollutants and climate variables which may impact the outcome of the effects. Some of these confounders may or may not be controllable. For those that are not controllable, like the climate variables, the potential changes in their variations in the future (like the regional changes in climate patterns) need to be taken into consideration in standard setting. I applaud the IRP for pointing out the need to consider uncertainties and limitations of evidence and assessments in establishing the standard.
Specific comments: Line 6 on p. 17, "reduce" ought to be changed to "alter" because alternative levels etc. need not only reduce estimated exposures and risks.

Ch. 4. General comments: Again, the role of climate change needs to be highlighted more since this will be the reality of the future. Both the effects of tropospheric ozone on climate change and the impact of climate change on the ozone health effects on human and the response of vegetation and ecosystem to ozone exposure need to be explored. Climate change also has an impact on the PRB concentrations. In particular, increased methane emissions from the permafrost and increased isoprene emissions from the biosphere with increasing temperature will have a direct impact on background and regional ozone concentrations, respectively.
Specific comments: The role and bio-mechanism of adaptation (lines 11-12, p. 29) needs to be explored further. The literature in this topic may be rather limited but this is the subject that needs to be better understood. The findings based on use of biomarkers also need to be explicitly included as a separate bullet point on p. 29.

Ch. 5. General comments: In the human health risk assessments, the validity of using the PRB concentrations need to be first established. Most epidemiological studies constructed models relative to the local mean pollutant concentrations. The resulting models may not be valid if the baseline concentrations are shifted, especially in light of the potential adaptation effect. An investigation of this approach is necessary to improve the credibility of health risk projections.

Ch. 8. Specific comments: The statement that "in general, a monitor need not be representative of the ambient air quality across an area of any specific size to be eligible for comparison to most NAAQS" (lines 12-14, p. 65) needs to be qualified. At least, the notion that some rules must be followed needs to be mentioned.

Graham (Dr. Judy Graham)

Generally, the draft is excellent. Congratulations to the authors for all the thought and hard work that went into this. My comments hopefully offer some small improvements. Specific comments follow.

1. There are several places that would benefit from a close editorial-level review
2. P15, footnote 7. This defines susceptibility and vulnerability. The definitions are fine, but are they necessary. They will be difficult to keep track of. Later on, they are misused somewhat. Why not just use one term that covers everything.
3. P 15-17. This sets out issues and questions. There is a lot of overlap between p15 and 16, but this is a consideration for ease of future IRP's, NOT a request to change this one. In any case, both groupings should explicitly call out the question of relative contributions of O3, photochemical oxidants, and other co-occurring pollutants to observed health effects. Some of this is implied (e.g. p16, L26-27), but as the input of epidemiology to the O3 NAAQS increases, there is an increasing need to attempt to dissect out the O3 contribution to the effects.
4. P21, L15. This section refers to discussion of "important older studies." This section should be revised since the language implies that such work will only be "discussed if they are open to reinterpretation… and/or to reinforce…conclusions." I strongly disagree with what is written. The NAAQS must rest on the ENTIRITY of the database. The newer material contributes in 2 ways: to reinforce the current standard or to show cause for a change in the current standard. Thus, the new material cannot stand alone. Also, the tendency will likely be to emphasize newer work, perhaps inappropriately. For example, suppose there is an "old" body of work showing lung cellular remodeling at 0 .25ppm and a new study comes along at 1ppm showing the same thing. The older work should have the discussion space, with the newer work only cited in a table, perhaps. One should be able to read the stand-alone document and think about an appropriate dose-response (or NAAQS) and not have the knowledge drivers relegated to a table or guidance to read the last document.
5. P24, L26. I suggest revision or deletion of this sentence. Indeed it is difficult to extrapolate from rats to humans for SEVERAL reasons, but not one reason (core temperatures) as stated here.
6. P24, L20ff regarding the cut point for animal studies. I fully support having a 1ppm cut-off for considering the literature. That level was selected 3-4 CD's ago because it captured all the classes of health effects. It greatly simplifies the literature review effort and simplifies the text of the document. The text goes on to say (L29ff): However, in recognition…studies using near ambient concentrations of O3 or other pollutants do not necessarily reflect… sensitive populations, studies at higher exposure levels may be included when they provide information [on} unreported effects…potential mechanisms, …exposure-response… or other wise…" "Additionally, some in vitro studies may provide information …on mechanisms …" Including papers above 1ppm should be exceedingly rare (in fact, I would suggest not even spending the time to review them for inclusion—you have plenty of work to do otherwise) for several reasons. In addition, the purpose of the IRA is to be brief, so adding discussion of work not relevant to ambient defeats that purpose.

a. 1ppm is NOT near ambient. It is already very high relative to ambient (justifiably so because of extrapolation issue).
b. Mechanisms can be extremely important, especially when seeking understanding of causality or interpretation of adversity. However, knowledge of mechanisms that will NOT occur at near ambient is only an academic exercise. For example, if frank edema occurs at 2ppm, what is the meaning of any mechanism studied at that level? Focus on MOAs that are operative at near ambient (<1ppm).
c. In vitro is even more removed from the real-world because homeostatic mechanisms are very likely to be missing, as are other mechanisms. Before using in vitro, there should be some kind of crude dosimetric evaluation to approximate what the in vivo related concentration might have been.

7. P 26 L 13 on QA. The plan discusses the CASAC review process in several places, emphasizing that it will review the main text of the IRA, but not the annexes. Somewhere, the Plan should explain how the annexes are peer-reviewed and how HERO, as related to O3, is peer-reviewed. This gets at the issue of ensuring that the most appropriate papers were selected for inclusion in the main text of the IRA.
8. P27, L7. Consider inserting "spatial and temporal" before "distributions."
9. P28, L16. Inflammatory should be deleted here because it is not an "additional" endpoint. It has been an endpoint for over 30 years.
10. P28 L19. An example of the confusion of terminology. It should include "vulnerable" to cover the outdoor workers.
11. P30, L25 ff. This section is on MOA. The bullets that follow on p31 get into extrapolation. Indeed, MOA is VERY relevant to extrapolation, but the bullets cover the whole of extrapolation, beyond MOA. Consider a separate section on quantitative animal-to-human and normal human-to sensitive human. This section would have a dosimetry component and a sensitivity component.
12. P31, L14. Since this says susceptible and vulnerable, outdoor workers should be added to the list.
13. P41. L4ff. This section refers to using APEX. My next comment is a "heads-up", not a suggestion for revision. EPA should examine the degree to which the evaluation of APEX is consistent with the NRC recommendations for model evaluation (*Models in Environmental Regulatory Decision Making.* Committee on Models in the Regulatory Decision Process, National Research Council, The National Academies Press, Washington, DC (267 pp, 2007). This report was sponsored by EPA. Because APEX is so important to the risk assessment, there is a high likelihood that someone will ask a question about its evaluation.

Grantz (Dr. David Grantz)

This document does a nice job of laying out the planned review and staff is to be commended for this work. I have a few suggestions for improvement.

1. There is a tendency throughout the document to assume that further review of the literature will reveal a lower exposure threshold for ozone effects. It may be, but the document should remain neutral in this regard. For example on page 16, line 2, this should be phrased in terms of a reevaluation of the threshold rather than a search for effects at lower exposure levels than previously observed.

Similarly, the document should avoid value judgments regarding the direction of changes and simply note the direction and probable magnitude of such changes. For example on page 20 at the bottom of the table incorporating welfare effects, the phrase "deterioration of property" could be changed to "effect on property." On page 34, line 18 the reference to "ecosystem stress" could be changed to "ecosystems effects".

2. There is a tendency throughout the document to emphasize and even specifically identify new publications as opposed to older and more solid research findings. It is important that older data that establish important effects receive appropriate consideration, particularly on vegetation effects in which much of the literature is older. On page 21, lines 15-20 it is explicitly stated that older studies will be specifically discussed <u>if</u> they are open to reinterpretation. A clause should be inserted here stating that older studies will also be considered if they remain definitive, or informative in interpreting newer studies, or otherwise relevant to policymaking. For example on page 57, line 8, staff is correct to focus the review more broadly than on crop yield. However, it is also important to explicitly recognize that the most complete data regarding vegetative systems have been obtained with crops. A clause is required here to specify that the agency will continue to include the crop data in their welfare analysis. On Page 53, line 25-26, staff has done a good job of referencing the older OTC data obtained during the National Crop Loss Assessment Network program and it is important that EPA continue to consider these data.

Along with the inclusion of crop loss data and mechanistic information obtained with crop species, it is important that the economic analysis envisioned with the FASOM model be applied at a sufficiently small scale that local variation in air quality is brought to bear on yield assessment.

On page 53, line 8, the Gregg et al 2003 study is a relatively weak example of the potential power of natural gradient studies. In this case the plants actually grew better in the more polluted environment. There are other studies that better capture the implications of natural gradients, including those dealing with Ponderosa pine in California, that could be cited here.

On page 57, line 2, the potential effect of ozone on pollination, through scent trials and volatiles emitted by plants, is not yet a well-established effect of ozone and is a poor choice to single out as an important impact.

3. Large scale effects on ecological systems should take precedence over smaller scale effects on individual plants or biochemical systems. For example on Page 22, line 11-13, the clause "and ecological or welfare effects" should be moved up to line 11 following the phrase

"animal toxicological studies". In general throughout the document the smaller scale studies should be seen as contributing to mechanism plausibility for significance of larger scale ecological impact. This is analogous to the approach taken for health effects. Similarly, on page 25, lines 27-29, it is stated that larger scale "ecosystem structure, function, and services" will also be considered. These should be primary and not secondary considerations.

On page 33 line 17 an additional bullet point should be added under ecosystem services to reflect the effects of climate change. On page 30, top of the page, a bullet point should be added relating to climate change and interactions with health effects. On page 32, lines 24-29 the potential ecosystem and other welfare effects should be spelled out in additional detail. For example the sentence beginning "this will include evaluation" on line 25 can be amended to read "…of ozone exposure on productivity and biodiversity of ecosystems, on yield and quality of crop systems, and on potential impacts on services such as CO_2 sequestration, watershed protection, wildlife habitat, and greenbelt issues.

4. On page 49 line 18 the reference to interactions between ozone and local meteorological conditions and climate should be modified to specify the types of interactions and their implications for (presumably) ecosystems effects. Similarly, lines 19 and 20 should better define what this complex relationship refers to.

5. Page 49, line 22-26. The description of the assessment methods and approaches considered should be amplified considerably, since the current document is the planning document. It is not optimal to wait for these approaches to be explained in the Scope and Methods Plan in 2011. Again, on page 55, line 9, as this is the planning document, it is important to describe briefly how the agency proposes to fill in the gaps in rural ozone monitoring, and what approaches the agency plans to take for enhancing the fusion of monitoring and modeling data.

Page 58, line 13. The issue of monitor probe height in rural ecosystems is significant but is not adequately explained here. Additional information is needed on the problems expected because of height of available ozone measurements, and the expected ramifications with respect to risk assessment. Finally any approach that the agency intends to pursue to address this problem in the admitted absence of sufficient information should be explained here.

6. Page 54, top of the page. Crop-Risk assessment is not well explained here and how C-R information will be obtained and applied remain unclear. Similarly on page 54, line 13-14, the limitations of the AGSIM modeling environment and how the agency proposes to address them could be more fully explained.

There are repeated references in this document to the 12 hour W126 metric, but there is no explanation as to why this metric was chosen over the many others that have been considered. This needs further explanation (pp. 51, 54).

7. Page 51, line 21. Reference to the overlap between 8 hour and 12 hour forms of the standard are unclear. The definition of the overlap is not obvious from the sentence.

There are inaccuracies on page 53, line 19 and following. The reference to compounding of effects appears to suggest that these would be more severe in mature trees than in seedlings and saplings, but actually the reverse is true. Page 56, line 15, the decrease in stream flow in

forested ecosystems referred to in this section depends on total tree water use, not on water use efficiency. Water use efficiency is generally defined as the ratio of carbon uptake to water loss and in itself has no effect on water flow.

8. Page 64, line 22, it is useful to reference the potential differences in ultraviolet and chemiluminensence-based monitors. However in this planning document it is important to describe what these differences may be and the ramifications for interactions with other ambient contaminants. In particular this discussion should be used to illuminate the discussion on the following page regarding the ability of ecosystem scientists to use other types of monitoring systems that are more portable for description of effects in remote areas.

9. A few minor comments:

Page 51 line 5, the phrasing "it under predicted higher" is awkward and should be reworded. Page 53, line 24 and page 54, line 5--reference to "then" and "at that time" require some specification of a date. On line 22 the awkward reference to "agricultural crops and fruit and vegetable species" can be changed to "agronomic and horticultural crop species." Page 55, line 17, the word "adjust" could be changed to "simulate" or something else that does not suggest that the basic data are going to be altered. Page 57, line 28, the phrase "will <u>once more</u> evaluate" is somewhat negative. The words "once more" can be eliminated.

Neufeld (Dr. Howard Neufeld)

I would like to commend EPA staff for putting out a quality document for our evaluation. Rather than repeat the comments of my colleagues, David Grantz and Peter Woodbury, I will detail those items that I picked up on that have not yet been emphasized in their summaries. However, I will occasionally re-iterate a point to emphasize its importance.

First, just two typos I found:
Pg 15, line 21 – change "susceptible" to "susceptibility"
Pg 24, line 7 – "lag of effects" should be just "lag effects"

Pg 21 – I agree with Dave Grantz that older studies should be discussed if their work remains definitive. As Dave emphasizes, much of the vegetation literature is "older", yet it is still the best work done to date.

Although I didn't mention it during the conference call, on page 25, lines 27-28, the document refers to ecosystem services and functions. These are never explicitly defined, and perhaps should be. On page 33, lines 17-20, they are more explicitly laid out, but it seems an eclectic selection at best. Why were these ones selected? Are "services" the only ecosystem attributes that are of consequence? Earlier the document mentions functions. What functions? Should items such as the tightness of nutrient cycles, energy balances, and so on, be included? These concepts should be clarified.

On page 51, the document specifies a 12 hr W126 exposure metric. Dave has already questioned why this particular metric, and I would add, why only 12 hrs? High elevation ecosystems are subject to elevated ozone for nearly 24 hrs/day and there is some evidence that plants can open their stomata in the dark (or fail to close them), making them prone to ozone uptake at these times. Furthermore, there is some suggestion that biochemical defenses may be reduced at night because of their dependence on current photosynthates in the day.

The *overlap* comment on line 21 is confusing and should be cleared up.

Gradient studies need careful review. Gregg et al., to their credit, went to great lengths to try and pinpoint a lack of ozone as the main factor causing greater growth in a more polluted area (due to greater ozone scavenging by NO_X in the city). But gradient studies done in the field, rather than with potted plants, can suffer from an inability to assign single-factor causation because there are simultaneous multiple environmental gradients that cannot be statistically separated. Nonetheless, with proper caution, they can yield some useful information.

When assessing economic risks, we need to consider that farmers may have switched to more resistant crop varieties, and that past estimates of the economic impacts of ozone due to lowered productivity may have to be adjusted. Along these same lines, ozone can have impacts on the genetic make-up of a population which is not evident to the eye (as foliar injury is, for example), so we should not ignore this hidden cost of ozone. This is particularly important in wild populations of plants, for which we have little background data on genetic variability.

I further support the use of the NCLAN data since those studies remain perhaps the best multi-species crop studies done with respect to ozone impacts.

I agree that the oxidation of floral scent story, while intriguing, remains untested at this time, so I would not overly emphasize it yet. I understand further experiments are being conducted to test the speculations resulting from those initial studies.

Monitor location and height are important on a local scale, and with forests, impacts will be hard to assess unless we know the depletion of ozone through the canopy to the forest floor. This varies with forest type, season, topography, and so on, and perhaps is an area in need of further investigation.

Finally, there may be trends where peak concentrations of ozone are becoming less frequent, and the baseline ozone is rising, making moderate ozone exposures relatively more abundant. How this changing ozone dynamic will affect plant responses (where one mantra has been that the high ozone concentrations have greater effects than lower ones) is yet to be determined.

Thank you for the opportunity to make these comments.

Foster (Dr. W. Michael Foster)

Summary Comments on Section 5.5.2 **Approach to Health Risk Assessment Based on Controlled Human Exposure Studies**

This section of the document overviews the planned review as staff understands and appreciates controlled human exposure studies. I have a few suggestions that may be helpful or perhaps to be taken into consideration.

- Maximal expired volume during the initial second of a forced expiratory maneuver from maximum lung capacity (FEV_1), is a single mechanical lung index, and perhaps the most basic to collect, as an indicator of a health effect. This index is the basis of the analysis proposed in Section 5.5.2.

- Initial acute influences of exposure to ozone in chamber studies upon the airway are reflective of airway and lung irritant responses, and not unlike the similar effects of many inhaled irritants leading to cough.

- Acute changes in the FEV_1 have little relationship, nor prognostic value, with airway inflammation that results in humans exposed in laboratory studies to ozone. This has been known for some time; in fact there is an inverse relationship in humans exposed to ozone whereby the smaller the decrement in the FEV_1 mechanical index, the more severe is the ongoing lung and tissue inflammation that results.

- Lung and airway inflammation and hyperreactive airways responses, indices and outcomes that do not develop acutely, do not correlate with FEV_1 changes, are however present 3 to 30 h post-exposure, and have been demonstrated and validated in numerous laboratory studies of humans. These health outcomes are of key concern, as represent delayed injury and inflammation to the airway and lung, and are appreciated as the major clinical features leading to emergency room visits, and hospitalization that ensue post-exposure during ambient exposure to ozone.

- Whether FEV_1 effects have any relevance, and/or airway and lung effects related to tissue inflammation and bio-marker responses, are more reflective of exposure to ozone, it is now completely accepted that host (genetic) factors have higher indices of success for predicting human susceptibility to adverse health response. Identifying host factors with relevance and predictability to health outcomes would enable risk assessment of the population.

- Endeavors or sponsorship to model mechanical and irritant derived effects (i.e., FEV_1) from previous laboratory studies as proposed in Section 5.5.2., would

seem to have little value or impact with regards to protecting segments of the population. Validity and reproducibility of human laboratory exposure studies to date, with genetic, pulmonary inflammatory, and airway reactivity outcomes, are more supportive of a basis for advice/consultation as EPA re- reviews a policy plan for action.

Ultman (Dr. James Ultman)

This document is well-organized and clearly written. I especially appreciated the summary of the previous exposure and risk assessment that the new review will be build on. Most of my comments regard some details that I feel should be added to the IRP. My only technical suggestion (and it is a general one) is that any new method that is used for analysis in the risk assessment be validated.

Detailed Comments

Page	Lines	
21	15-16	What will form the basis of reinterpretation of the older studies? Given the importance of clinical studies at low exposure levels, it would be particularly useful to perform meta analyses that include all (new and old) relevant data sets.
22	17-21	Please give the specific cut-off date for inclusion of new studies.
24	17	State the specific populations that will be studied. How were these population identified?
27	11-13	Please give a short list of oxidants that will be considered in addition to ozone.
40	28-29	What approaches in addition to the quadratic roll-back method will be considered. How will the quadratic roll-back and other possible approaches be validated?
41	17-18	Why do cities in the Northwest appear to be excluded from consideration?