January 29, 1999

EPA-SAB-CASAC-LTR-99-001

Honorable Carol M. Browner
Administrator
U.S. Environmental Protection Agency
401 M Street SW
Washington, DC 20460

> Subject: Review of the Office of Research and Development's Ozone Research
>   Needs Document

Dear Ms. Browner:

The Clean Air Scientific Advisory Committee (CASAC) of EPA's Science Advisory
Board, supplemented by expert consultants (together referred to as the "Panel"), met on
November 16, 1998 to review the March 31, 1998 draft document, "Ozone Research Needs to
Improve Health and Ecological Risk Assessment" (EPA/600/R-98/031), in a public meeting in
Research Triangle Park, NC. At the meeting and in the written comments of Panel members
provided to EPA staff, the Panel assessed the adequacy of the draft document as a statement of
research needs regarding the health and welfare effects of atmospheric ozone. Key issues raised
by the Panel's are summarized below. More detailed comments are contained in the attached
report and appended comments, and in the transcript of the meeting.

The Panel would like to express an overriding concern that it considers more important
than comments pertaining specifically to the draft document. It was the consensus of the Panel
that the Agency should develop and sustain a substantive, well-prioritized and integrated program
of research on the health and welfare effects of ozone. The present level of research and the likely
funding portrayed by EPA Staff falls far short of an adequate effort. The Panel proposes the
recommendations for particulate matter research developed by the National Research Council as
an example of the scope of integration and prioritization that the Agency needs to apply to ozone
information needs. Information on the scope, costs, and time dimensions of an adequate ozone
research program is crucial to ensuring that the program is appropriately linked to the Agency's
budgeting priorities and to the Agency's schedule for review and promulgation of the ozone
standard. The Panel also noted the likely importance of co-pollutant effects, and encourages
greater integration of research strategies for ozone, particulate matter, and other air contaminants.
The Panel did not consider the draft ozone research needs document in isolation, but rather in
view of its value in helping to frame such an analysis.

Additional integration of the information contained in the draft document is needed to
provide a useful basis for development of an ozone research strategy. The draft document
appropriately notes a number of important research needs within numerous categories, but does
little to integrate or prioritize the needs across categories. The document is comprised of two

independent sections consisting of two workshop reports, one on health and one on plants and ecosystems, which were developed using different approaches and are formatted differently in the document. Neither section integrates research needs or priorities adequately across categories and the Executive Summary does little to integrate the information across the two reports.   The addition of an integrative overlay to each section and to the Executive Summary, perhaps developed by EPA staff together with the workshop rapporteurs, would greatly enhance the value of the document.

The value of the document could also be enhanced by the addition to the Executive Summary of a brief description of the information playing a key role in decisions regarding the ozone standard at recent reviews. The present document provides little sense of the factors influencing recent decisions and the key issues remaining unresolved at those times. Those critical information gaps provide a platform from which the extensive list of current questions regarding the health and welfare effects of ozone can be developed into a prioritized list of research needs which, if met, would significantly improve the basis for future reviews of the standard.

In summary, the Panel strongly urges the Agency to develop an ozone research strategy that prioritizes information needs and describes the resources and time required to meet those needs. The Panel views the draft research needs document as identifying a number of appropriate unanswered questions regarding the health and welfare effects of ozone, but strongly recommends that the effort be expended to improve the description and justification of critical information gaps and to integrate the prioritization of research needs across categories and between sections. Although publication of the two workshop reports has some value, the value of the effort to EPA and other researchers and research sponsors can be greatly enhanced by attention to the issues raised above and in the Panel's more detailed comments. CASAC would be pleased to review a revised ozone research needs document and a draft ozone research strategy.

Sincerely,

/signed/
Dr. Joe L. Mauderly, Chair
Clean Air Scientific Advisory Committee

CASAC REVIEW OF DRAFT OZONE RESEARCH NEEDS DOCUMENT

1. Introduction

The Clean Air Scientific Advisory Committee (CASAC) of EPA's Science Advisory Board, supplemented by expert consultants (together referred to as the "Panel"), met on November 16, 1998 to review the March 31, 1998 draft document, "Ozone Research Needs to Improve Health and Ecological Risk Assessment" (EPA/600/R-98/031), in a public meeting in Research Triangle Park, NC. This meeting follows the completion of the CASAC's scientific and technical peer review of EPA's Air Quality Criteria Document for Particulate Matter PM), and its Staff Paper on PM. The purpose of the research needs review is to engage Agency staff and the public in a dialogue concerning research that will be needed in support of the next Congressionally mandated particulate matter national ambient air quality standard (NAAQS) review cycle.

The 14 Panel members were each assigned specific sections for review and comment (See Table I - Discussant Assignments), but encouraged to review the entire document. Each of the

Table I - Discussant Assignments

Section #	Section Title	Lead Discussant	Associate Discussants
Part I - Health Risk Assessment			
2	Exposure Assessment	Wolff	Hopke, Middleton
3	Controlled Exposures	Lippmann	Upton, McClellan
4	Dosimetry/Extrapolation	McClellan	Lippmann, Mauderly
5	Epidemiology	Vedal	Ayres, Lippmann
Part II - Crops, Forests and Natural Ecosystems			
3	Methodology	Jacobson	Legge, Pell
4	Mode of Action/ Species Response		
5	Modifying Factors		
6	Exposure Dynamics		
7	Role of Modeling	Legge	Jacobson, Pell
8	Ecosystem Response		
9	Scaling		
10	Economic Assessment	White	Elston, Legge
11	Monitoring/Modeling	Middleton	Wolff, Hopke

sections other than the Executive Summary and the introductory sections of the two workshop reports were assigned a primary reviewer and multiple secondary reviewers. These individuals were asked to summarize their comments verbally at the meeting, and then the section was opened for additional comment and discussion by the entire panel. EPA staff are directed to the attached written and verbal comments for the complete critique of the draft report. The body of this report summarizes selected key issues, but does not reiterate all comments of the Panel.

2. General Comments

2.1 Charge to the Panel

The October 16, 1998 letter to the CASAC Chair from Dr. Lester Grant, Director of the National Center for Environmental Assessment (NCEA), Research Triangle Park, NC, transmitting the draft document did not contain a charge to the Committee, requests for attention to specific issues, or specific questions. Thus, the Panel of CASAC members and consultants reviewed the document from their individual perspectives on its adequacy as a foundation for developing a strategy for research to mitigate key information gaps regarding the health and welfare effects of ozone.

2.2 General Issues

2.2.1 Intentions of the Agency Regarding Ozone Research

The Panel expressed serious concern about the lack of evidence that the Agency intends to develop an ozone research strategy and to conduct a substantive program to mitigate key information gaps regarding the effects of ozone on human and plant health. The Panel raised this concern from the viewpoint of its consensus that ozone remains a criteria air pollutant of important concern for both its individual effects and its effects as a co-pollutant with particulate matter and other air contaminants. Together, the lack of timeliness in summarizing research needs after the last review of the ozone standard, the small size of the existing ozone research portfolio, the small budget for ozone research portrayed by EPA staff at the meeting, the lack of identification in the draft document of the key information gaps at the last review, and the lack of effort to integrate and prioritize the research needs identified in the two workshops were taken as evidence that the Agency does not envision conducting a substantive program of ozone research in preparation for the next review of the standard. Indeed, this was confirmed when staff told the Panel at the meeting that the Agency does not have a plan to develop a formalized strategy for ozone health effects and exposure research.

EPA staff outlined the Agency's current ozone research as consisting of a single, although large, epidemiological study, a plant and ecosystem program at its Corvalis laboratory, atmospheric research done through the efforts by NARSTO, and research on particulate matter that might include ozone as a co-pollutant. The Panel expressed its view that the small current effort on exposure assessment and the near absence of effort involving controlled exposures of

humans and animals represented important deficiencies. The Panel noted that the Agency's intramural research resources provided good capabilities for such research, and expressed concern that those resources had been directed so completely toward research on particulate matter.

The Panel recognizes that substantial attention and resources are currently being directed nationwide toward research on particulate matter, and understands the potential for that effort to detract from research on other pollutants. The Panel emphasizes, however, that important information gaps remain concerning the effects of ozone, and cautions that inattention or lack of timeliness in defining the most important gaps and resolving them can only increase the difficulty the Agency faces at the next review of the standard.

As the sole document presenting the Agency's perspective on ozone research, the present draft is inadequate by failing to describe the scope, time dimensions, and projected cost of the research effort required to meet important information needs. Information on the scope and time dimensions of prospective research is crucial to ensuring that the research program is appropriately linked to the Agency's schedule for review and promulgation of future ozone standards and implementation of control programs. Information on projected costs is needed by the Administrator and other senior Agency officials to place ozone research needs in perspective relative to other priorities in the Agency's budgeting process. Information on costs will also be of interest to Congress as it evaluates competing requests for scarce financial resources. The 1998 National Research Council report on Research Priorities for Airborne Particulate Matter provides an excellent example of an approach to developing and conveying the range of information needed for an ozone research strategy.

Overall, the Panel does not view as acceptable the Agency's apparent lack of intention to move forward at this time with development of a formalized ozone research strategy, or an integrative research strategy for ozone together with other pollutants.

2.2.2 Approach to Developing the Research Needs Document

The job of summarizing ozone research needs was only partially completed, and not in a timely manner. The majority of the Panel views the document as it presently exists to have limited value.

The document consists of the binding together of reports from two workshops conducted independently. The formats of the two workshop reports differ, but neither contains an integration of the information developed by the several working groups in each workshop. As a result, there are duplicative statements of research needs and no prioritization of needs across categories (working groups). EPA staff noted at the meeting that the Agency recognized that the two workshops and their reports differed and had debated whether or not to bind them into a single document.

An Executive summary was added to introduce the two reports, but it does not identify the key information gaps that existed at the last review of the standard, it does not adequately integrate the information contained in the reports, and it presents no summary prioritization of needs across the two reports. As a result, the present draft is limited largely to a listing of uncertainties about the effects of ozone.

To become an effective starting point for developing an ozone research strategy, the information in the draft document requires an overlay of effort to integrate the information and prioritize research needs. The Panel was told at the meeting that additional integrative information was provided by working group rapporteurs. Subsequent to the meeting, the Panel received copies of the rapporteurs' reports from the four working groups of the health workshop. A review of these reports suggests that they would be a useful starting point for better integration of the information and prioritization of research needs within and among the four health areas.

In many cases, too little information is given to inform the reader why a research need received the priority it was assigned relative to other needs.

The two workshops were conducted in March and May 1997. The draft is dated March 1998, but it was not submitted to CASAC for review until October 1998, a year and a half after the workshops. The value of the identification and prioritization of research needs for ozone and other criteria pollutants would be greatly enhanced by beginning the process immediately after the review of the standard, perhaps as a natural extension of the development of the Criteria Document.

3. Comments by Section

3.1 Executive Summary

The Panel did not engage in an extended discussion of the Executive Summary beyond its lack of portrayal of key information gaps at the last review of the standard, and the role this section should play in addressing the integration and prioritization needs described above. It was the general view that this section would be largely re-written in an appropriately revised document.

*See **Appendix A** for individual comments by Dr. Mauderly.*

3.2 Research Needed to Reduce Uncertainty in Health Risk Assessment for Ozone

3.2.1 Introduction

No summary comments.

*See **Appendix A** for individual comments by Dr. Mauderly.*

3.2.2 Exposure Assessment

Overall, this section does a good job of identifying important research needs, but additional information would be useful to define the needs in more specific and descriptive terms.

There is a need to integrate research on the assessment of ozone exposure with research on exposure assessment for other pollutants. Overall, the potential role of ozone as a co-pollutant together with other criteria and non-criteria pollutants should be emphasized more throughout the document.

There is also a need to integrate, or at least coordinate, this information with that in the epidemiology section. Most of these needs are related to obtaining better information for epidemiological studies of ozone effects; thus, the two sections need to be complementary.

Research needs 4 and 5, on pages I-18 and I-19 would seem to be more appropriately listed in the Controlled Exposure Section

One of the present limitations of the assessment of personal exposure to ozone is the difficulty of making measurements on an individual basis. The need for developing a practical personal monitor for ozone should be mentioned as a research need.

*See **Appendix A** for individual comments by Dr. Hopke, Mauderly, Middleton, and Wolff.*

3.2.3 Controlled Exposures in Humans, Laboratory Animals, and In Vitro Test Systems

Controlled human and animal exposure studies have provided a large portion of the key information we presently have on the health effects of ozone, and the Panel urges the Agency to include such work as a strong part of their ozone research program. The five priority 1 needs, one priority 2 need (unlabeled as such on page I-33), and three priority 3 needs comprise a menu of needs that is very comprehensive, but broadly described and poorly focused. A very high priority should be given to controlled exposure studies of normal and susceptible humans, and perhaps the second highest priority should be given to chronic studies in non-human primates.

*See **Appendix A** for individual comments by Drs. Lippmann and Mauderly.*

3.2.4 Dosimetry and Interspecies Extrapolation

This section describes dosimetry research needs in reasonably well-developed, concise, and comprehensive manner, and the relative assignments to priority 1 and priority 2 categories are appropriate. Several of the priority 1 needs are interrelated, and could be addressed effectively in an integrated manner.

The description of research need 4 (anatomical data) should be edited to clarify that better interspecies information on the effect of anatomical path length for ozone delivery to the respiratory tract is needed.

*See **Appendix A** for individual comments by Drs. Lippmann and Mauderly.*

3.2.5 Epidemiology

It is appropriate that the need for improved epidemiological assessment of the chronic effects of ozone is given high priority. The long-term effects of ozone remain a key uncertainty. While the study of young adult lungs in the Los Angeles area is appropriately noted as a <u>type</u> of study which is needed, it is important that future studies address the lack of controls and specificity of the histologic findings that severely limit the value of this example study. The development and epidemiological use of biological markers more specific for ozone exposure and effects is an important associated need, and one that might be addressed by controlled exposure research. It is not clear that there is information suggesting that cardiovascular disease should be a focus of research on the chronic effects of ozone.

There were mixed views regarding the importance and likely benefit of additional research on the relationship between ozone and daily mortality and morbidity. It may be appropriate for the existing database to be reviewed by an independent group, as done for particulate matter, to explore alternate interpretations before investing in additional data collection.

Some of the research needs mentioned in this section, such as numbers seven and eight, deal with exposure assessment, and would more appropriately be covered in that section.

Research needs three through six might be more appropriately assigned to the priority two category.

*See **Appendix A** for individual comments by Drs. Vedal, Lippmann, and Wolff.*

3.3 Research Needed to Assess Ozone Effects on Crops, Forests, and Natural Ecosystems

The discussion of this portion of the report largely ranged across the numerous sections simultaneously rather than proceeding section-by-section as done with the health portion. Staff is directed to the individual written comments of the assigned reviewers for comments that were offered on specific sections.

The reviewers were somewhat confused by the approach taken to developing this half of the report. First, the difference between "research issues" and "recommendations" was not clear. Second, it was not clear that the order in which the recommendations were listed was to be taken as the order of priorities, as finally explained by staff at the meeting. Many of the

recommendations appeared to focus on the need to develop studies or design experiments, rather than describing specific information needs. The Panel noted that the document would most appropriately focus on describing key information gaps and justifying their prioritization, rather than describing studies. Overall, the specific information gaps and their priorities were portrayed far less clearly than in the health section.

As was the case with the health portion of the document, the current information needs were not adequately framed within the context of information gaps at the last review of the standard and how the additional information might impact the next round of decision-making.

The Panel expressed skepticism regarding the need to develop exposure chambers for plants that simulated all of the variables that occur in the environment. The value of experimental exposures often lies in the ability to control exposures precisely and eliminate variables in order to test hypotheses. Skepticism was also expressed regarding the value of foliar injury for assessing damage from ozone, both in linking foliar changes specifically to ozone effects and in linking foliar injury to plant health and economic outcome.

It was not clear that current information gaps are preventing development of a rural ozone monitoring network. Such a network would have two values, assessing the dose-response for crop loss due to ozone, and gaining a better understanding of the background levels of ozone.

In assessing the economic impacts of ozone on plants and ecosystems, it may be appropriate to consider "non-use", or aesthetic, values as well as "use", or direct damage, values. Another consideration that is not mentioned, but which might be questioned, is the possible value of ozone-resistant plants as an ozone sink.

See *Appendix A* for individual comments by Drs. Elston, Legge, Pell, White, and Wolff.

Appendix A

Individual Written Comments of Panel Members

Note: These are individual comments from Panelists and do not necessarily represent Panel consensus positions. Some of these comments were obtained from electronic (fax, e-mail and scanned) files, therefore, some minor translation errors may still be present.

Dr. Joe L. Mauderly, DVM

General Comments

1. No context is given for this document. We are not told in the introductory material how this document will fit into the development and maintenance of the Agency" ozone research program. Indeed, we are not told if the Agency plans to sustain a significant program of research on ozone at all. This is perhaps the most important overall issue, and one that supercedes the importance of the critique of this document. Ozone is considered to be one of the most important criteria pollutants with regard to both human and plant health. The Agency needs to develop a plan by which meaningful research on the human and plant health effects of ozone is conducted despite the current political and scientific emphasis on particulate matter. The apparent lack of a plan to do so is another manifestation of the failure of our current mode of considering, and studying, one pollutant or pollutant class at a time.

2. It would be useful for the introductory material to include a brief summary of the principal findings that drove the setting of the past two standards for ozone. This would provide a foundation for the logical sequence of considering whether or not the same issues are considered the principal "drivers", whether or not we now have an adequate understanding of those effects (ie, plausibility, mechanisms, exposure-dose-response relationships, magnitude of national health and ecological impact) and thus, the existing research needs. Without this background, it is difficult for the reader to frame a correct view of the current status of our understanding.

3. A major problem with this document is that it consists of the binding together of two workshop reports with an almost complete absence of a summary or synthesis that extends across the two reports. While this approach is acknowledged by the Agency, the acknowledgement doesn't mitigate the fact that the approach does not result in an adequate presentation of current research needs. The two sections (workshop reports) are structured differently. There is no synthesis of research needs and priorities across categories even within each report, much less across the two sections. Apparently, the workshops were planned and conducted without thought that the reports would contribute to a single document. A step is missing; the Agency did not undertake an overlay synthesis that would meld the information into a single, easily understood document.

4. Research priorities are presented independently for a number of topics in each of the two sections. This results in a large number of "number one" priorities. Although listing research needs is an important step, prioritizing them is also important. The Agency acknowledges this by presenting priorities; thus, it cannot state that the document was not intended to prioritize the needs. Once committed to prioritization, the Agency should carry the job through at least one more step. That would be the synthesis of a list of priorities that span each section. That level might be acceptable, but a synthesis across the two sections is really needed as well.

Specific Comments

<u>Executive Summary</u>
P E-1, l 19: Exposure doesn't "entail" health effects, it <u>produces</u> them.

P E-2, l 16: The workshops might have prioritized needs within the two general areas but if so, these priorities are not presented in the document. Did this really occur, and if so, what happened to the results?

P E-3, l 24: Different "disciplines" are mentioned several times in the Executive Summary. Care to tell us what disciplines you had in mind?

P E-4, l 10-11: All pollutants have subtle effects – what's special about ozone in that regard?

P E-6, l 6: Do a universal search for the word, "insure". Here and almost everywhere else, you really mean <u>ensure</u>.

P E-6, l 25: If exposure measurement error is important, why isn't it listed as an exposure priority? Is that the same as "exposure assignment" error?

Health Research Needs

<u>Introduction</u>
P I-1, l 27: Changes at the anatomical level reported would not increase measured small airways resistance, because of the minimal mass flow at that level.

P I-2, l 3: I know of no evidence that environmental ozone exposure has caused, or could cause, "severe, progressive changes" that would result in the effects listed.

P I-6, l 11: Are you uncertain about the marked increase in asthma? Why do you say it "may" be increasing?

P I-8, l 2: The foregoing material just stated that epidemiology can't characterize the health burden. What do you mean here by "characterize"?

<u>Exposure Assessment</u>
P I-13, entire section: You need to define "exposure" and "dose" up front, and stick with those definitions. They sometimes get confused in this section.

P I-16, l 9 (heading): The terms, "statistical level" and "causal level" are not adequately defined in this section.

P I-16, l 27: Why is there no value in also conducting studies in places and at times where the NAAQS is not exceeded? I'd argue with this philosophy.

P I-19, l 18: This research need more appropriately fits in the controlled exposure section.
P I-24 (and in other charts): Are the "number one" priorities in order; ie, is the first one listed considered a higher priority than the second?

Controlled Exposures
P I-29, l 11: This seems an example of PM-related tunnel vision. Why wouldn't one envision that PM would enhance the effects of ozone as well as the opposite?

P I-30, l 20: What in the world is a "normal sensitive" individual?

P I-31, l 4-5: How does one study "repair and remodeling" in human subjects?

P I-33, l 4: The "Priority 2" heading is missing here.

P I-33, l 23: It is not clear how this research would differ from that performed to meet other research needs. How is this different?

Dosimetry
Overall, this is probably the best-written of the sections. Little editing is needed.

P I-45, l 20: It is not stated clearly that information on anatomical path length is included in this research need. Path length is very important, and it should be called out clearly.

P I-46, l 15: Data on unrestrained animals are important, but isn't it also important to get better data on "unrestrained" humans during various activities? Do we have enough information on that?

Epidemiology
P I-59, l 19: Isn't this research need covered in the exposure section?

P I-61, l 1: Again, isn't this need in the exposure section, or shouldn't it be?

Ecological Research Needs
P II-7, l 20: The acknowledgement of duplication simply points out a deficiency in the process. Duplications should have been sorted out.

P II-8, l 11: It should be "study of crops, etc.".

P II-10, l 8 (and other sections): Are the "recommendations" listed in order of priority? Are they all of first priority rank, or what?

P II-11, l 23: Presumably, you mean <u>site</u> instead of "cite".

P II-16, l 20: Most readers probably won't know what "mesic" means. I don't', and it's not in my trusty dictionary.

P II-18, l 27-29: It was stated, or strongly implied, in the foregoing material that injury occurs from stomatal uptake. Now cuticular uptake is discussed. Please sort out for the reader the presumed importance of the various exposure pathways.

P II-30, l 2: Why would the model run for 400 days instead of a year?

Mr. John Elston

I am responding to your request to comment on EPA's draft documment Ozone Research Needs to Improve Health And Ecological Assessments (EPA/600/R-98/031).

Please note that I am in agreement with the CASAC panel general conclusion that within the Context of each of the scientific workshop proceedings (Public Health and Ecological Risk) there needs 1) an overall ozone research mission with specific research strategies neccessary to address each of the listed topics; 2) a prioritization of of those strategies; and 3) a "state-of-the-art" summary of where we are currently for each of the the strategies so that the reader can make reasonable judgements on where to place added emphasis. In summary a "grand" organization is needed.

More specifically, with regard to my assigned topic, economic research, I suggest: 1) differentiate and indicate separate analyses for evaluting "use and non-use values"; 2) incorporate the value of public perception (i.e., visibility) into the non-monetary discussion; 3) determine if it is possible to place a value on endangered species (i.e., Cost of extinction!); and 4) if certain plant species can absorb ozone without any apparent effect what is the likelihood, economically that such species can be considered as a biocontrol method and thus be cost beneficial.

Dr. Philip Hopke

Exposure Assessment
The EPA Administrator wisely promulgated new NAAQS for both ozone and particulate matter at the same time because of the recognition or the substantial interrelationships between these two pollutants. There is currently a major expansion in the research program on particulate matter, and it is important that these studies include important co-pollutants like ozone. Similarly, the ozone program needs to be carefully coordinated with the PM program. In the exposure assessment part as m most of the document, the needs for ozone research are presented in very broad terms and generally described as focusing only on the ozone measurements with co-pollutants only being included as the 9th topic in the Priority I research needs. There are co-exposures suggested in topic 4 for controlled exposure experiments. However, it would make

more sense to integrate the exposure assessment program more intimately with other copollutants particularly PM. The research topics listed are the traditional list of topics that have been presented over arid over. It seems to be the time for a more explicit plan to be developed that indicates more specific goals that can be accomplished within the time and budget constraints that are likely to apply over the next 5 years. The topics as presented are appropriate areas of study, but really do not provide a clear prioritized set of specific needs that will really inform the development of the next ozone criteria document and provide improved confidence that we can set a NAAQS for ozone that will effectively protect public health.

Monitoring and Modeling
The monitoring and modeling issues are presented in the ecosystem part of the document and are not integrated with the health effects research needs. It is important to take this document as a starting point arid develop an integrated set of needs that address both the health and ecosystem effects from ozone and the co-pollutants that are simultaneously present in the atmosphere. The document is silent on one of the most important problem with the modeling efforts which is the quality of emission inventories in most of the United States. There are major uncertainties is the emissions from both anthropogenic and biogenic sources. We clearly need a more extensive network of monitors in non-urban areas if we are to be able to assess the effects on ozone on ecosystems arid crops. These monitors can potentially be useful in conjunction with IMPROVE and other remote area PM monitors. These would provide data for testing regional scale models although they would have only limited value without more detailed chemical speciation. There need to be statistically valid personal exposure studies in order to provide adequate test data for exposure assessment models. There are modeling and measurement needs at both urban and rural scales for exposure assessment for both health arid ecosystem/crop effects. Without better measurements of the rural ozone concentrations, it will not be possible to extend the exposure/effect studies to the broader population and thus, the effects cannot be adequately quantified.

Dr. Eva J. Pell

Methodology
In my view the most important methodological need is to determine "how to scale up", and how to interpret data from experiments with smaller and/or younger plants when predicting effects on older and larger organisms. This theme permeates recommendations in many sections of the document. Clearly, we understand little about the implications of ozone exposure on natural and managed forests, and only by addressing this issue will we get there. From an economic point of view, these systems are of great importance.

I am less persuaded about the value of searching for the perfect chamber. Similarly expending significant resources to determine the accuracy of the open-top chambers and resultant NCLAN data is probably of less value than addressing the issue discussed above. I am in favor of developing new methods and evaluating current methods, but in a context. For example when addressing issues related to factors which modify plant response to ozone it would be possible to

try different designs and protocol, thus learning more about plant response while considering the way it is being studied.

In several sections including the methodology section there is a great deal of emphasis on determining how foliar injury relates to effects. I have never been persuaded that this is an approach worthy of high priority. It is certainly true that if foliar injury could be a predictor of economic effects it would be very useful. But investing in this avenue of research suggests some certainty that such a relationship exists. It is my view that (a) there probably are other stresses which will mimic the type of lesion induced by ozone; hence, identification of "ozone injury" may be a risky business; and (b) it is very possible that depending on plant sensitivity you can lower plant assimilatory capacity or pollen viability, for example, without ever inducing visual injury.

Mode of Action
I am comfortable with this section and believe that if developing superior methods and predictive models is a long term goal, then establishing an understanding of how this gas exerts its toxic effects is essential. I concur with the priority of recommendations and would emphasize the value of developing a better understanding of the fundamentals surrounding ozone flux. Response of guard cells to ozone impacts both the uptake of the pollutant and associated uptake of carbon dioxide which is essential for photosynthesis.

Factors That Modify Plant Response
This sections fits reasonably with the important issues in the Methodology, Modeling and Scaling sections.

Exposure Dynamics
I see recommendations 2 and 3 as preceding recommendation 1. You really need to be able to estimate ozone flux both at the leaf and stand level before determining the meaning of exposure indices.

The Role of Modeling in Assessing Ozone Effects
I suggest that recommendations 1,2, 5 & 6 are the important recommendations. These recommendations get at the heart of issues that include an iterative process of model and system evaluation. Here modeling addresses the issue of scaling. Lastly, the modeling recommendations acknowledge the importance of having a mechanistic understanding if models are to stand a good chance of being predictive.

Ecosystem Response
There are several recommendations which seem highly relevant particularly 3,4, 6 and 8. The major issues touched on here relate to how ozone affects nutrient cycling and the issue of ozone as one stresses amongst many. The latter is also discussed under the section on *Factors Modifying Plant Response*. In this section there also appear two recommendations, numbers 4 and 6, that deal with determination of ozone effects on biodiversity, and on wetland and desert species. These are large ecosystem questions that have been almost completely neglected.

Scaling
These recommendations are redundant with those appearing earlier. I find recommendations 1 and 2 the most compelling. Again I am unconvinced about the emphasis on relating foliar injury to important plant responses. Utilization of direct measures of biomass would be more instructive. To attribute changes in biomass to ozone exposure will require the use of models which account for other major determining factors including, e.g. water and nitrogen.

Dr. Sverre Vedal

CASAC Review of the Ozone Research Needs Document

Part 1. Section 5: Epidemiology
In general, this is a very thorough research needs assessment that could benefit from improved focusing on the most critical needs, as well as some combining of needs. Furthermore, one or two important needs are underemphasized. When thinking about ozone epidemiologic research needs, one should consider most seriously the type of work that is likely to truly advance our understanding of ozone health effects, as well as work that is in some degree innovative. Performing more of the same types of studies that have been performed merely to add to the "weight of evidence" is, in my opinion, less desirable.

The most critical ozone "research need" is to evaluate the long-term effects of ozone exposure in humans. It is therefore appropriate that addressing this need is assigned the priority 1 need for epidemiological studies. The external review draft makes several mentions of the importance of findings from a lung histology study of young accident victims in Los Angeles (Sherman, 1991). This is a very important <u>type of study</u> that is needed to make one all important link between the animal studies of long-term ozone exposure and the human epidemiological studies of purported long-term exposure effects. Unfortunately, this particular study from L.A. was uncontrolled, and the histologic findings described were nonspecific. The findings are therefore uninterpretable. First, then, considerable weight should be given in the document to the need for rigorous studies of this type that can be interpreted with respect to long-term ozone exposure.

Another type of epidemiologic study that needs more emphasis in the needs document, and which has the potential to more directly test the effects specifically of long-term exposure, is one that assesses health outcomes in populations With similar current ozone exposure, but considerably different long-term exposures previously. This study design ensures that any observed effects are not due to recent exposure. The West Point, the Yale (Kinney) and the Berkeley (Tager) studies are examples of this type of study. The problem with such studies is that it is not clear that when effects are observed, that they can be attributed specifically to ozone exposure, since settings with high ambient ozone concentrations also typically have high concentrations of other pollutants. Nevertheless, negative studies of this type would be interpretable, and some positive studies might also be interpretable depending on the setting. Second, then, more emphasis should be placed on the types of epidemiologic studies that take this approach.

The only other need that I would like to include as Priority 1, of those listed, is to identify the independent effects (that is, independent of other pollutants) of long- term ozone exposure and short-term exposure. The problem here is that I believe that epidemiology has only limited ability to do this successfully, although studies from complementary settings may offer some hope. Because of this difficulty, I would not include these studies as first priority.

The final need that I would include under Priority 1 is to utilize biological markers of ozone exposure in epidemiologic studies in order avoid the vagaries of ozone exposure measurement based on ambient concentrations. The problem here is initially to identify relevant markers that can be feasibly used in an observational study.

Additional specific comments on each recommended research needs section:

1.   Long-term exposure effects: Attempts to perform epidemiological studies on populations that have experienced decreasing concentrations of ozone over time are unlikely to be very informative. First, it is unlikely that populations that have experienced significant decreases in concentrations will be found. Second, it is difficult to imagine that studies on changes in some health outcomes over time would be interpretable with reference to ozone effects. It would be preferable, as noted above, to focus on people moving to areas of different concentrations rather than focusing on regions with changing concentrations. I would not include cardiovascular disease under this need, since the evidence for such effects is weak at best, and dilutes the focus of this research need.

2.   Lift-shortening studies: Given the controversy over the recent epidemiology of particulate matter, in which studies were performed that are much like those proposed to address this need, it is unlikely that pursuing this tack for ozone is going to provide much, if any, conclusive evidence.

3.   Exposure metrics: This is a very difficult issue to address with epidemiologic data. Various metrics tend to be very highly correlated, making it difficult to determine which are the most relevant measures. Determining appropriate (or improved) ozone exposure metrics should therefore probably be in the Priority 2 group of needs. "Non-anthropogenic" ozone needs to be clarified. Is this due to ozone generated from non-combustion hydrocarbon sources, or atmospheric ozone drawn down to the troposphere? Presumably, regardless of the source, the effects of ozone should be the same. This must then refer to the contribution of these' non-combustion ozone precursors to ozone exposures.

4,   Independent and interactive effects: Although this should belong in the Priority 1 group of needs, the difficulty of performing epidemiological studies that can effectively address issues of independent pollution effects, or interaction effects, should not be underestimated. It may be that the only feasible way in which this can be done is through studies performed in different settings with varying pollutant mixes, again taking an example from particulate matter epidemiology. The problem with this approach is that the populations in different settings are different, making some

compansons across setting difficult. The interactive effects with aeroallergens in asthma would be particularly interesting.

5.　　　Sensitive copulations: This should include other morbid conditions besides asthma, given the observations in some studies of an association between daily ozone concentrations and total mortality.

6.　　　Relationship between acute and chronic effects: I have difficulty comprehending what, with respect to epidemiological studies, is actually being suggested here. There is no obvious application of these interesting observations to epidemiologic studies. It should not be in the Priority I group, and I would drop it as a need until it is clear that this is relevant.

7.　　　Central vs. other monitoring sites: Much of this work comparing fixed site and personal monitoring correlations has already been done, and is being done in the USC studies.

8.　　　Measurement errors: The issue of exposure measurement error and its effects is common to all air pollution epidemiology and is very important. This need and #7 above should be combined.

9.　　　Exposure response relationship: I am not sure if further epidemiological studies, of the type that has already been performed, are going to provide much useful information on the dose-response relationship. Again, the comparison with particulate matter epidemiology is appropriate. As has been seen in the PM work and in the few ozone studies in which it has been addressed, these studies will typically find a linear concentration-response relationship that extends to the lowest concentrations observed. Performing studies in settings with very low concentrations may be more helpful in defining the effects at low concentrations.

10.　　　Short-term effects on cardiovascular outcomes: I don't believe many would postulate that the adverse effect of particles is based on "hypoxia and its consequences", as noted here.

11.　　　Knowledge of diseases caused bv ozone exposure: To propose that learning more about the diseases that ozone affects will improve ozone epidemiology is probably true. But is unlikely to focus the research. This need should be dropped.

Based on both need and feasability, I would group the epidemiology research needs in the following way:

Priority 1:　　1.　　Effects of long term ozone exposure
　　　　　　　　- lung histology studies
　　　　　　　　- West Point, Yale, Berkeley type studies
　　　　　　2.　　Biomarkers of exposure
　　　　　　3.　　Sensitive populations
Priority II:　　4.　　Independent and interactive ozone effects

5.   Various ozone exposure metrics
6.   Measurement error
   - central sites vs. other sites vs. personal exposures
   - statistical issues
7.   Cardiovascular outcomes
8.   Concentration-response relationship

Dr. Warren White

COMMENTS ON OZONE RESEARCH NEEDS

Personal circumstances limited the time I was able to put into this document, so I restricted my attention to Part II. My overall comment is that this document reads like what it is: an incompletely edited collation of bullets from two workshops. Considering my inexperience in this topic area, I was disappointed at how little I found that I couldn't have generated *a priori:* non-specific calls to consider interactions between variables, for more cooperation between researchers, for improvements in every area. I doubt that this document merits the expert-hours and jet fuel that are being spent in the present review.

5.   FACTORS THAT MODIFY PLANT RESPONSE

Do the two paragraphs of introduction, taken together, say anything more than the following?

> Plant response to oxidants must be understood as a function of factors both internal and external to the plant. Internal factors include genetic makeup and developmental stage. External factors include weather, competition from other plants, the presence of pests and pathogens, and other pollutants and agricultural chemicals.

11-14, lines 5-10
The genetic makeup (e.g., cultivar) and the developmental stage play critical roles In the way individual plants respond to ozone and other external stresses. Whereas the magnitude of response of a particular species or variety depends on external environmental factors such as...

What is the distinction being drawn with this "whereas"? Is it between the individual and the population? Between internal and external factors?

11-14, lines 15-16
The issues are ozone versus environmental stressors, degrees of importance, and ranking of stressors,

Does this say anything more than that you'd like to rank the various stressors by their importance? To the degree that they may be synergistic as you suggest above, can you necessarily expect to succeed? If a plant can survive A or B but not both, which stressor is the more important?

11-14, line 19
...drivers of atmospheric conductivity...

We talking lightning bolts here?

11-16, lines   13-14
(2)   Long. term studies in forest systems should further understanding of the range of responses of seedlings, saplings, and mature trees In stands and forests to ozone.

This is formulated as a recommendation rather than an issue. As an issue it might read "Long-term studies in forest systems are needed to understand the range of responses

As a recommendation, it is so vague as to be meaningless. It can be read as anything from a platitude to an action item:

    (2a) [Existing] long-term studies in forest systems [can be expected to] further understanding of the range of responses

    (2b) Long-term studies in forest systems should [be initiated in order to] further understanding of the range of responses -

    (2c) [Ongoing] long-term studies in forest systems should [be refocused toward] further understanding of the range of responses

11-17, line 28
(9)   There are a number of reports in the literature that indicate ...
More studies of this type are needed ...

No! We don't need more <u>studies</u> of this type. We presumably need information not yet obtained by studies of this type. What is the missing information?

8.   ECOSYSTEM RESPONSE

The research issues in this section are parodies of scientific bureaucratise.

11-25, lines 4-6
Criteria used to determine the parts the life cycle of a tree that should be investigated . . . should be determined.

This sentence swallows its own tail.

11-25, lines 6-12

As community-level studies proceed, It will be necessary to follow ecosystems over long time periods. Forest health monitoring is a good example of this type of study. Other critical research should include long-term ecosystem studies, strengthening the current Forest Health Monitoring Program.

No wonder the report seems interminable!

11-25, line 21
The significance of stress-induced outcomes must be evaluated as to their severity
Prolixity strikes again.

11-25, line 27-28
Visible foliar injury, as an endpoint, could suggest that no foliar injury be considered acceptable.

Again, don't be afraid to go back and erase the beginning of your sentence if you thought of a better way of expressing your meaning halfway through, and incorporated that in the ending.

11-25, lines 29-30+
There was considerable discussion of the need to conduct research on important relationships between foliar injury, tree function and growth, previsible physiological effects, carbon budgeting and allocation, and predisposition to insect and disease attack.

I think you mean ". . relationships [of] foliar injury [to] tree function and *growth, previsible physiological effects," etc. i.e.,* you are concerned with the relationship of foliar injury to everything else, not of everything to everything. And our need is to understand, not "to conduct research".

11-26, lines 6-7
Included are the dynamics of leaf area index, carbon fixation, and ozone effects on net carbon acquisition and associated respiration effects.

That's a lot of dynamics and effects, and what is it they're included in?

11-26, 12-13
Of concern also is the possible loss of individual species within populations and between species within a community (i.e., loss of biodiversity) from exposure to ozone.

I think you mean to distinguish loss of individuals within populations from loss of species within a community.

11-26, l3-l5

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Changing root/shoot ratios, vegetative structure, species composition, and year-to-year variation have been related to changes in growth and reproduction.

This is a tautalogical statement, carrying no non-trivial information.

The recommendations on 11-27 are refreshingly succinct. But (6) has no evident connection to any of the enumerated research issues. And (8) is focused only by the qualifier "on managed forests." If you *added* a similar recommendation "on croplands", and another "on unmanaged ecosystems", you would be recommending all possible research on plant growth.

10.   ECONOMIC ASSESSMENT

This chapter is better than some others, because it actually contains some non-trivial statements. One is issue 4; *the economic valuation of crop losses from ozone exposure is relatively well known when compared with other potential valuation Impacts.* Another is issue 5: *With a few exceptions, loblollypine in particular, estimates of the economic effects of ozone on managed forests are not based on a sound understanding . . .* Unfortunately these firm conclusions, which would seem useful guidelines for research planners, didn't make it to the recommendations section.

Much attention is given here and elsewhere to potential interactions between ozone and other stressors. Recommendation 7 is to *Develop economic valuation techniques that will permit separation of the effects of ozone from other stressors as they interact to cause damage . . .* Likewise, issue 2 observes *that Existing economic valuation techniques may not be capable of discerning the harm to ecosystems solely and directly caused by exposure to ozone.* The problem, however, is that any apportionment of economic damages among significantly interacting causes is unavoidably arbitrary, dependent on convention rather than advances in valuation techniques. If a plant can survive A or B but not both, then what do we mean when we attribute specific damages to A or B? The inherent limitations of cost-accounting as an analytical framework should be acknowledged.

Issue 6 claims that *The potential harm of ozone exposure to individual plant species in natural ecosystems is understood in terms of foliar injury, plant physiology,* etc. This seems contradicted by issue 3 of Chapter 8, which states *Ozone responses are known for only a few native plants; no data is available for the great majority of native species.* And if we don't know the ozone responses of most native species, then the economic analyses developed under recommendation 2 are not going to be able to measure *changes in the value of natural ecosystems.* Economic sophistication doesn't replace data.

Issue 3 notes that *Harm to threatened and endangered flora and fauna deserve special attention because of their protected status under the Endangered Species Act. In* fact, this "special attention" is in the form of a constraint that must be imposed outside the utilitarian framework of

the usual welfare accounting. The limitations of the utilitarian framework are suggested in recommendation 3, but should be more explicitly recognized.

Dr. Stephen Ayres

My comments on the need for additional ozone research follow the conversations I initiated when we met together at Raleigh. Some of the comments seemed quite unusual to many of the members and I hope that some of my suggestions could be seriously debated.

As you know, I have been involved in the relationships between environmental pollution of the ambient air since 1965 when I served on Mayor John Lindsay's task force on clean air. Since then there has been a good deal of study on the various criteria air pollutants, studied separately, but little attention on important linkages to that effect human health. I made the perhaps outrageous suggestion that some of EPA's efforts be aimed at the etiology of chronic pulmonary disease and asthma rather than the pollutants themselves. of advantage of dealing with ALL of the possible environmental contaminants, including physical stressors such as heat and cold, which could be causative agents.

The reason this has not been seriously considered in the past is in part on the contaminant background cf most regulators and the paucity of lung scientists who have dedicated themselves to identifying the causes of chronic pulmonary disease and asthma. I feel strongly that only a tight collaboration between the environmental scientists funded by the EPA and the lung scientists funded by the Pulmonary Division of the National Heart, Lung, and Blood Vessel Institute could cost-effectively deal with the needed research approaches. Indeed, much of that information is already available in the separate programs. I would strongly suggest that the EPA and NHLBI sponsor a national a national symposium around the question: DO AIR POLLUTANTS CAUSE OR SIGNIFICANTLY EXACERBATE CHRONIC PULMONARY DISEASE?

The cancer society has been very successful in assembling the talents of a broad array of experts in studying the cause and treatment of cancer. I would propose that the EPA marshal the services of pulmonary disease specialists, immunologists, lung injury experts, geneticists, cell biologists, epidemiologists, lung pathologists, and others.

Spirometry in all of its transmutations and morbidity and mortality indices have been quite useful in pointing the finger at particulate and ozone pollution as causal agents of lung disease. They lack both specificity and sensitivity, however, and new indicators of effect must be identified.

Very little attention, for example, has been given to studying morphologic changes in the lung in people living under various environmental conditions. Newer techniques of lung inflation and morphometry, aided by scanning and transmission electron microscopy can identify subtle changes in lung structure. A national registry of lung sections removed from the lungs of accident victims, supported by epidemiologic questioning, could produce a good deal of useful information.

Ptimate exposure studies with these types of sophisticated evaluation could supplement the morphologic approach.

Many years ago, Ishikawa, Bowden and Wyatt (Arch Env Health 18.60-666 1969) studied using advanced methods of lung preservation studied lungs in Winnipeg and Saint Louis. They showed the combined effects of air pollution and cigarette smoking and demonstrated what could be done with innovative studies of lung biology. I do not believe that these etudes are much quoted or replicated.

I am not suggesting we ignore the study of individual air pollutants. I am only pointing out that such studies can never help us identify the irritant mix that must be responsible for the evidence of Lung injury that has been reported since the earliest episodes in cities such as London.

Dr. Jay Jacobson

1. Part II is a compilation of research issues and recommendations that seems to have two main objectives: a. to recommend research that supports EPA regulatory needs and b. to recommend research suitable for the environmental missions of other governmental agencies.

2. The document should clearly state that the research issues and recommendations are listed in priority order within each major topic.

3. I agree with the research objectives listed in 3.2.1 regarding open-top chamber studies with the exception of the statement that actual exposures should mimic ambient conditions. As soon as a chamber is used, ambient conditions are affected. The question is to what extent the response to ozone is influenced by the changes in ambient conditions. For many but not all purposes, the changes may be insufficient to undermine the aims of the experiment.

4. I agree with the items listed in priority order in section 3.2.2 Use of Chamberless Designs. An important missing component, however, is the need to match ambient conditions such as sunlight, temperature, rainfall and soil conditions across gradients of ozone deposition. This will greatly restrict opportunities to use this approach and it is necessary to know the degree to which ambient conditions are similar among sites. The section is deficient if it doesn't make this point.

5. There is a mismatch between the research needs section and the recommendations section (3.3). Some research needs are not listed under recommendations and some recommendations are not discussed in resarch needs.

6. I do not agree with recommendation no. 2 that methodology should be developed for verification and validation of NCLAN data. It's time to move on and focus efforts on new and improved research approaches rather than trying to use resources to validate experiments that were completed years ago.

7. The research issues and recommendations in section 4 seem appropriate with the exception that no. 4 in section 4.3 seems to me to be the same as recommendation no. 3.

8. The priority arrangement of recommendations in section 5 'Factors that Modify Plant Response' seem reasonable with the exception that I would give a higher priority to no. 8, the influence of climate change on response to ozone.

9. In section 6 Exposure Dynamics, I have difficulty with the wording of the first recommendation. The 'best' exposure index depends on the criteria applied. It already seems abundantly clear that there is no one statistic that will serve for all species under all conditions for all end-points and be acceptable from a policy perspective. This wording sets up an impossible goal.

10. In general, the report would benefit from improvements in clarity and organization. Providing a brief statement of what is known for each research issue followed by recommendations would give readers an understanding of what has been accomplished as well as what needs to be done. Better explanation of the need for the individual research items would greatly improve the value of this report.

Dr. Allan Legge

I have reflected on my initial written comments and the discussions which took place at the November 16,1998 CASAC Meeting in Chapel Hill and feel that more focussed written comments would be more appropriate. The emphasis will be on Part II, "Research-Needs to Address Ozone Effects on Crops, Forests, and Natural Ecosystems". My initial comments were born out of frustration. As I indicated in my verbal comments at the CASAC meeting, I did not find the document to be of much use to EPA. Essentially, 'we' were presented with a research needs "wish list" which was formatted in a fragmented and piecemeal fashion. There was little or no justification for any of the research needs listed as well as no attempt at synthesis arid integration of the research needs. A critical point is that one was left with the impression that the plant/air pollution effects research community had not learned anything over the past 30 years and needed to start over. Additionally, as, noted by a number of the CASAC members, Part II was simply a report of the outcome of a workshop held in May, 1996 In Raleigh, NC. The above were the sources of my frustration.

When CASAC deliberated on the Ozone CD and- Staff Paper, a number of points were raised and uncertainties identified especially in the CASAC closure letters to -the Administrator of EPA. It would seem logical to me that these uncertainties would be 'prime' candidates for research and identified as such in the text of an "Ozone Research Needs" document so that the Agency could address these uncertainties in a timely fashion and be prepared for the next ozone review cycle in 2001-2002. This was not done in the text. Further, an inordinate amount of time has elapsed since the Ozone CD and Staff Paper were reviewed by CASAC and the 'Ozone Research Needs' document provided to CASAC for review. The Workshop on "Ecological Research Needs and

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Ozone" was held in May, 1997 while the Workshop on "Health Research Needs and Ozone" was held in March, 1997. The "Ozone Research Needs" document is dated March 31, 1998 but only given to CASAC for review in October, 1988 for open discussion in November, 1998. With respect to "Ecological Effects and Ozone" almost two years have elapsed. Valuable time has been lost. One is left with the sense that the Agency does not view the ozone effects issue as important. This was confirmed at the November 16,1998 CASAC meeting when very direct questions were required to determine what the "Agency" had budgeted for ozone research in fiscal 1998-99 and 1999-2000. The sense which I obtained from the answers to the budget questions was that the budget for fiscal 1998-99 was approximately $900,000 for ozone research for both health and ecological effects while the budget-for this research in fiscal 1999-2000" was 'ZERO'. The clear conclusion that one can draw from all of this is that the Agency will not be ready for the next ozone review in 2001-2002. I suspect that this would still be the case even if the Agency had an "Ozone Research Needs" document that it could use. The fundamental question is as follows: 'Why is the Agency not committed to health and ecological effects research given the uncertainties identified by CASAC in their review of the CD and Staff Paper and given the fact that ambient ozone concentrations are increasing with ozone being the most toxic of the criteria air pollutants?'. The Clean Air Act (CAA) is very clear as noted on page II-1 of the "Ozone Research Needs" document where the following is said: "'Any national, secondary ambient air quality standard, as defined under Section 109(b)2, must specify a level of air quality the attainment and maintenance of which in the judgement of the Administrator, based on such criteria, is requisite to protect the public welfare from any known or anticipated adverse effects associated with the presence of such air pollutant in the ambient air" (see lines 13-17). The key point is that it "is requisite to protect the public welfare from any known or anticipated adverse effects". By displaying a lack of commitment to health and ecological effects research related to ozone the 'Agency' has chosen to ignore their responsibility as defined under the CAA. It seems to me that CASAC should point this out very clearly or we will be viewed as part of the problem rather than helping provide the solution.

The above comments are harsh but in my view can help the Agency' regain the 'perspective' which it seems to have lost.

RECOMMENDATIONS:

The following is list of suggestions to help the Agency in the future.

1.   At the time of the review of the CD and Staff -Paper for a given criteria air pollutant, the staff of the Agency has an excellent command of the research which has been done and the research which is needed to reduce identified uncertainties. This is when the "Research Needs" document should be written.

2.   Given (1) above in terms-of timing, the 'Research Needs' document should provide a framework for research in a given area with the key uncertainties clearly identified as to where they fit into the overall framework.

3.	Given (2-) above in terms of framework, the "Research Needs" document should identify the linkages to other criteria air pollutants so that research efforts can be coordinated and made more cost effective.

4,	The "Research Needs" document must not be a 'wish list' of research projects -- but rather a document which reflects integration and synthesis of our understanding in the light of identified uncertainties which need to be addressed "to protect the public welfare from any known or anticipated adverse effects".

5.	More emphasis should be placed on interdisciplinary research within the "Research Needs" document. To say that there will be interagency cooperation is not adequate or sufficient especially given the Agency's reliance on risk assessment in decision making.

In summary, I found the "Ozone Research Needs' document with respect to Part II very unsatisfactory and in my opinion of very little use to the Agency in its current form. The inordinate delay in preparing the "Ozone Research Needs" document for review by CASAC and the apparent lack of commitment by the Agency to health and ecological ozone effects research given the inadequate budgets for fiscal 1998-99 and 1999-2000, will result in the Agency being unprepared for the 2001-2002 review of the ozone standard. The Agency needs to regain perspective on one hand and rethink its' approach to the preparation of "Research Needs" documents.

Dr. Mort Lippmann

REVIEW COMMENTS ON CONTROLLED EXPOSURES

Introduction and Background:

Research involving controlled human exposures to ozone have greatly influenced all of the revisions to the 1971 ozone NAAQS. The NAAQS relaxation of 1979 relied on a LOAEL of 150 ppb for a 1 hr exposure of exercising adult asthmatics (Delucia, A.J. and Adams, W.C. J. Appl. Physiol. 43:75, 1977). The 1993 NAAQS retention was based primarily on the absence of effects deemed adverse in numerous controlled human exposure studies to ozone in pure air lasting 2 hours or less at concentrations below 180 ppb, and discounting evidence for substantial effects on respiratory function at lower concentrations from several field studies (Spektor, D.M., et al., ARRD 137:313, 1988; AARD) 138:821, 1988), and one controlled 6.5 hr chamber study (Folinsbee, L.J., et al., JAPCA 38:28, 1988). The 1997 NAAQS revision placed a considerably greater reliance on the results of 6.6 and 8 hr controlled human exposure studies to ozone in pure air, documenting functional, inflammation, and airway reactivity responses at 80 ppb with moderate exercise during exposure, but also on the results of both numerous field studies of functional responses at very low ambient levels and on numerous macroepidemiologic studies showing increasing rates of hospital admissions for respiratory causes with increasing levels of ambient ozone concentration.

One lesson that can be drawn from this brief history is that controlled human exposure studies that ask some of the right questions, such as the influence of age and exercise level, as well as the extent of response in terms of a range of responses of interest (function, inflammation, airway reactivity, airway permeability, symptoms, performance) can be very valuable in showing the nature, extent and substantial interindividual variability of short-term responses in groups of relatively healthy individuals exposed to ozone in pure air.

Other important lessons derived from controlled human exposures to ozone in pure air include:

1) Different individuals are responsive in terms of the different endpoints.

2) The search for biomarkers predictive of responsiveness has been unproductive.

3) Functional responses are smaller in controlled exposures to ozone in pure air then for exposures to ozone in ambient air.

Controlled exposure studies in animals have also been highly informative. For example:

1) Short-term controlled exposures to rats can produce many of the same acute responses seen in the controlled human exposure studies, but require much higher ozone concentrations for comparable responses.

2) Subchronic 8 hr-daily controlled exposures of monkeys at 250 ppb have produced structural and functional changes that could be indicative of progressive and cumulative lung damage, and some changes are greater over 18 months with intermittent months of exposure as compared to continuous daily exposures throughout the l8 months.

Comments on Chapter 3 on Controlled Exposures in Humans, Laboratory Animals and in vitro Test Systems:

The chapter presents five Priority 1 needs, 1 Priority 2 need, and three Priority 3 needs that are each rather bland statements on things that it would be nice to know more about. There is, however, no indication why any one of them belongs in its assigned priority class. Also, each need is very broadly stated, with no indication of: 1) priorities within the need area; 2) promising approaches or opportunities to expeditiously or efficiently address the outlined need; or 3) which parts of the needs can best be addressed by controlled human acute-exposure studies, controlled animal acute exposure studies, controlled subchronic or chronic animal exposure studies, or in vitro exposure studies. This is a glaring deficiency in a document whose only possible utility is to guide the selection of studies that could produce useful results over the next 5 years.

With the very limited research resources that are likely to be available for ozone research over the next few years, the real questions should be:

1) What questions are the most important ones that EPA's Clinical Studies Branch can effectively address in its new and grand Chapel Hill facility?

2) What other controlled human exposure study objectives should be the focus of an RFA for STAR grants or cooperative agreements in the near future?

3) What chronic exposure studies in rats, if any, should the Toxicology group at RTP be conducting in the near future?

4) What will the focus of an RFA on the most critical issues for a chronic primate ozone exposure studies be?

5) Will any other ozone research resources likely be available for other high priority whole animal or in vitro studies? If so, what would the RFA specify for such research?

6) How will the various studies performed by the clinical research investigators, the animal inhalation investigators, and the in vitro investigators be coordinated so that the individual studies will provide a basis for the whole controlled exposure program to be greater than the sum of its parts?

7) How will the controlled exposure program be integrated with the dosimetry and epidemiology research to ensure that the most critical uncertainties about the ozone exposure-response relationships in humans be clarified for future NAAQS revisions?

From the nature of the questions that I posed above, it is evident that I believe that the menu provided in Chapter 3 is hopelessly comprehensive and unfocussed on really critical needs in relation to any realistic assessment of anticipated amounts of tine and resources. I would give highest priority to: 1) clinical lab studies that focussed on lavage and serum biomarkers that Correlate with responsiveness to the various effects produced by short-term ozone and mixed exposures to healthy and asthmatic individuals (as a means of getting at the mechanisms of response); and 2) chronic ozone-exposures in primates that extended the duration of intermittent ozone exposures and included measures of lavage and serum biomarkers at periodic intervals during the extended exposures (as a means of directly addressing the nature and extent of progressive chronic effects of long-term ozone exposure in a relevant animal model, and relating biomarkers of response to those determined in controlled short-tern exposures in the human volunteers).

REVIEW COMMENTS ON DOSIMETRY AND INTERSPECIES EXTRAPOLATION
M. Lippmann

The research priorities summarized in Chapter 4 on Dosimetry and Interspecies Extrapolation are reasonably concise, well developed, and comprehensive. The basis for priority assignment was

not made clear, nor was the distinction of the time-frame for the research. However, the assignments to Priority 1 and Priority 2 status seen reasonable.

Many of the Priority I needs overlap and could most effectively be addressed in a unified program of research. Based upon the need to address all of these high priority needs at an early stage of future ozone dosimetry and modeling research, and the high probability of, at best, only a modest amount of funding for this kind of research, attention should be devoted to the development of a more comprehensive multidisciplinary RFA for such research.

REVIEW COMMENTS ON EPIDEMIOLOGY
Lippmann

The research priorities summarized in Chapter 5 on Epidemiology are well targeted on important knowledge gaps and provide appropriate rationales for their implementation. There are, however, too many Priority 1 topics.

The first Priority 1 topic clearly deserves its prominent place. The second one, addressing lifespan shortening is clearly also a high priority area for research, but it is not at all clear how the influence of short-term exposures can be investigated. This topic should be more clearly focussed on the influence of longer-term cumulative exposure. The needs identified as #s 3, 4, 5 and 6 belong under the Priority 2 heading, along with #s 7, 8 and 9. The inclusion of needs 10 and 11 in the Priority 3 category seems to be appropriate.

An issue that is not addressed in this chapter is the feasibility of research focussed on the needs that are outlined. Some of these needs can be at least Partially addressed effectively by further analyses and regression of large data Sets that are already in existence (AIRS, fine particle network (1979-1983], mortality and hospital admissions by cause from federal and state data bases, population cohort outcome data [Am. Cancer Soc., Nurses Health Study, NHANES, etc.]) Such analyses can be performed at relatively modest costs, and can yield very useful information within 2-5 years. More definitive results will require the creation of new cohorts and the widespread collection of additional ambient air quality and personal exposure data at considerably greater costs and over a considerably longer time-frame (>10-20 years).

If the creation of new cohorts is possible, it would be highly desirable. If not, then research resources should be focussed on the attainable goals of analyses of pre-existing data sets, and these should he explicitly addressed and prioritized.

Dr. Roger McClellan

COMMENTS ON EPA DOCUMENT

Ozone Research Needs to Improve Health and Ecological Assessments

General Comments

1. There is a need for the Agency to periodically develop documents such as this one to describe research that has the potential for reducing uncertainties in the scientific database for the various National Ambient Air Quality Standards. Thus, the present document is of substantial value in providing a general context for research on ozone and other air pollutants. However, the long delay between issuance of the1 last Criteria Document and the Staff Position Paper and promulgation of the standard has left a period of time when SPA research on ozone may have drifted due to an absence of clear strategic direction.

2. The document identifies a number of general research objectives that might be pursued to reduce uncertainties in setting the National Ambient Air Quality Standards for Ozone. Descriptions of the objectives are generally very broad. The authors are to be commended for advancing some broad prioritization of the objectives, i.e., Priority 1, 2 and 3. However, the document in most cases does not provide adequate discussion of how the research findings arising from successfully addressing each of the objectives would really impact on the setting of the National Ambient Air Quality Standards for Ozone. While all of the objectives have scientific merit, it is very likely that they vary considerably and how the research would have potential impact on the setting of the ozone standard. In finalizing the document or developing the next iteration, the Agency might consider following the lead of the NAS/NRC Particulate Matter Research Committee and for each objective provide a statement on (a) scientific merit, and (b) potential regulatory impact.

3. A serious deficiency in the present document is that it fails to provide an adequate description of the time and scope dimensions of each of the research needs. It is likely some of the research could be accomplished in a year or two with a few person years of effort. Other research will very likely take five or more years to complete and require 50 or more person years of effort to complete.

4. A related serious deficiency of the document is the failure to justify the estimated financial resources required to carry out the needed research. The absence of information on financial resource needs renders the document almost useless for planning purposes within the Agency in developing the Agency's/President's budget and equally useless to the U.S. Congress in deciding on funding priorities for this research. The primary objective of the Agency's research program, in my opinion, should be to conduct "goal achievement" research in support of the Agency's regulatory mission. This requires planning at the research strategy level that demands information on financial resource needs. The failure of the Office of Research and Development to develop public documents that outline strategic research needs and the associated financial needs is an invitation to the Program Officers and the EPA Administrator to regularly "shortchange" the Agency's research program. I am disappointed that this document does not do anything to correct that deficiency.

5. The document tends to project a "silo view" of air pollution with an almost exclusive focus on ozone and a failure to adequately consider how health responses attributed to ozone are, in many cases, very likely responses to exposure to complex mixtures of ozone and other pollutants, especially particulate matter. The last review of the scientific basis for both the ozone and particulate matter National Ambient Air Quality Standards clearly indicated the need to avoid concentrating on single poUntants. The statements on page 1-8 of the present document attempt to explain away the document's failure to lay out a research strategy for multiple pollutant research. However, recognizing the importance of multiple pollutants, it is disappointing that the Agency again failed to seize the opportunity to provide a research strategy context for addressing the multiple pollutant issue. In my opinion, debate during the next round of reviews of the scientific basis for both the ozone and particulate matter National Ambient Air Quality Standards will very likely center on the multiple air pollutant issue.

In summary, the present draft is a useful start in outlining most of theresearch activities one can envision carrying out on ozone. There is something for everyone to address. Unfortunately, this approach and the lack of information on the projected scope, time schedule, and financial resource requirements of the research outline does not provide an adequate scientific justification for the kind of research program that is needed to address the ozone issue and its relationshipto other pollutants. Intuitively, I suspect that $25-5O million per year will be required over a 5-8 year period if the scientific community is to provide input for setting a science-based standard. In the absence of a science based standard, Isuspect that the alternative, a technology, will result. The estimated implementation costs and estimated health costs of the ozone standard and particulate matter standard would appear to justify a substantial research investment to ensure that these standards are science based.

Dr. Paulette Middleton

General comment. The report needs to be better integrated. I agree with Joe's requests in the letter of a few days ago calling for additional commentary on priorities and rationale.

Exposure. Priorities 1, 4 and 9 are highest on my list. They all address particularly important and less well understood areas. All are aimed at providing relevant information on exposure as it occurs in reality. They each begin to address the potential synergies of multiple stresses that exist.

Monitoring and Air Quality Modeling. Issue 10, dealing with communications and problem solving, should be turned into a recommendation.

EPA has been using a variety of models in studies of ozone and particulate matter. An in depth assessment of the appropriateness and applicability of the models in determining best management strategies is very important. Many states and other stakeholders will be developing approaches to deal with real and potential ozone violations. Guidance on model use is essential. This is not

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formally noted, however, it could be the most important barrier to directing defensible policy decision making.

Dr. George Wolff

I. General Comments

It is my understanding that the research "needs" document serves at least two purposes. First, it contains an outline for a long-term research program that addresses the major uncertainties and unanswered questions without consideration of the time frame. The second purpose is to prioritize the "needs" in order to maximize the reductions in uncertainties and to provide answers to some of the unanswered questions *before the* next NAAQS review. The present document is a collection of lists, which, if combined and integrated, might address the long term component. However, the second purpose is completely ignored.

II. Health Effects

It is apparent that the four different groups who put together the four lists did not communicate with each other as there is considerable overlap between some of the "needs" and no attempt to integrate them into a coordinated program.

An overriding concern for many aspects of the health effects program is the importance of background ozone. Based on relatively sparse data, the U.S. summertime continental background is estimated to be 0.03 - 0.05 ppm for both a 1-hour and 8-hour time frame. However, as indicated by the range, it is variable and it has a distribution that extends beyond this range. At least two epidemiology studies which found a statistical association between ozone and hospital admissions were conducted in locations (Spokane and Tacoma, WA) where the ozone concentrations were dominated by changes in the daily ozone background. For example, in Spokane the daily 1-hour ozone varied from 0.029 ppm (lower 10%) to 0.054 ppm (90%) and it was slightly lower in Tacoma. Consideration should also be given to background concentrations in controlled human and animal exposure studies. Control subjects should be exposed to background ozone concentrations rather than zero concentrations.

A.   Exposure Assessment

I think the key exposure uncertainties have been identified. It is not clear, however, how much the uncertainties will be reduced if the proposed research plan is carried out. It is not sufficient to just identify data gaps, but the question of how much new data are needed to make a difference in reducing uncertainty must be addressed. The other area that needs more consideration is how the various "needs" can best be addressed in a coordinated research program. It is my opinion that a number of the highest priority "needs" could be addressed simultaneously in a well designed research project that includes an epidemiology component. Let me elaborate on these points.

1.   I agree "need number 1" is the highest priority, but it poses some important questions which have not been mentioned. Which microenvironments do we need additional data for? How much data do we need for a given microenvironment before we have reduced uncertainty to a comfortable level? What is a comfortable level? How many comparisons between "statistical-level" and "causal-level" relationships do we need until we have enough? Until these questions are addressed, we cannot design an effective research plan for "need number 1."

2.   "Need 2" is also a top priority, but again a program cannot be designed until an assessment of how much new data on activity patterns and breathing patterns are needed. We know that data on activity patterns are sparse and this probably introduces one of the largest uncertainties to the risk assessments. However, a determination of how much data are needed to reduce this uncertainty must be addressed first. Also, the focus should be on the populations of concern: outdoor children and asthmatics.

3.   "Need 3" is also a top priority and the questions that first have to be addressed are how many geographic locations, which ones, arid how much data need to be collected. The locations should be chosen because they are representative of larger areas of the country so that we can minimize the number of areas needed to characterize the maximum amount of the country. For ozone, the studies need to only focus on the summer. Also, the focus should be on the populations of concern: outdoor children and asthmatics.

4.   "Needs 1, 2, 3, 6 and 7" have common data needs that should make them amenable to an integrated study. Although "need 3" will have other geographic components that can be done separately, one of the geographic areas could be used to simultaneously address "needs 1-3, 6 and 7." In addition, they should be integrated with simultaneously occurring epidemiological studies.

5.   It seems to me "need 4" belongs in the controlled human exposure category rather than the exposure assessment. It also is a "need" that is on a longer time-frame. It is a complex issue which will not likely produce meaningful results in a 5-year time frame of the time frame of a NAAQS review. Consequently, as an ozone exposure assessment "need," I give it a lower priority.

6.   "Need 5" also seems more like a controlled human exposure issue.

7.   "Need 8" needs to be more clearly articulated. The acute component is addressed in the daily time series epidemiological studies and in the summer camp type studies. However, it is not clear how the Agency intends to address the chronic component. Also it is not clear how or why we need to differentiate between the health effect contributions from anthropogenic and now anthropogenic caused ozone.

       Certainly the acute component of "need 8" is important, but it will be addressed elsewhere. The remaining parts of this "need" appear to me to be a low priority.

8.   Referring to "need 9," I agree that it is important that measurements of other potentially important pollutants be measured and included in the statistical analyses used to determine relationships between concentrations and health endpoints. All present and future studies should incorporate such measurements as part of the standard protocol. Consequently, such measurements should be included in the efforts to simultaneously address needs 1-3, 6 and 7. However, I question why PAN was singled out here. In all previous CASAC reviews, PAN was never cited as a health concern at the levels typically observed.

9.   I agree that "needs 10 ands 13" are lower priority, but not "needs 11 and 12." Data for "need 11" (aeroallergens) should be collected as part of an asthma epidemiological study occurring simultaneously with the measurements to address "needs 1-3, 6 and 7." Concerning "need 12," I recommend that the Agency examine the ozone and PM trends in the South Coast Air Basin. Significant improvements in air quality have occurred since the l960s.

B.   Controlled Exposures

What are the priority 2 issues?

C.   Epidemiology

1.   I believe that "need 2", the statistical association between ozone and daily mortality is the top priority because that will be the prime focus of the next review if it holds up. A data base should be generated and made available to several different groups for rigorous independent analyses. Ideally, this should be coordinated with the exposure assessment project so that issues of exposure and exposure misclassification are also addressed.

2.   Not included as a "need" are reanalyses of the ozone/morbidity time series data. Unlike the PM studies, none of these studies have ever been examined by an independent group to see if alternative explanations exist. In addition, the exposure assessment program could be a source of a rich new data base that could be made available. I believe these types of analyses are needed because the studies that found similar statistical associations between ozone and hospital admissions at background concentrations, as compared to the studies carried out in the eastern U.S. cities, raise questions concerning the causal nature of these associations.

3.   "Needs 7 and 8" are high priority exposure assessment "needs" that hopefully will be addressed by that program.

II. Ecological Effects

As with the health section, this section is made up of lists of needs by nine different groups with no attempt to develop an integrated program.

An overriding concern for all aspects of the ecological effects program as well is the importance of background ozone. Based on relatively sparse data, the U.S. summertime continental background is estimated to be 0.03 0.05 ppm for both a 1-hour and 8-hour time frame. However, as indicated by the range, it is variable and it has a distribution that extends beyond this range. Consequently, the determination of the background distributions would be one of the goals of a rural monitoring network. I do not believe we have any information of the background ozone distribution for a measure like SUM06. In addition, background needs to be considered in chamber and field exposure studies. Background concentrations, not charcoal-filtered air, should be used for the control plants. Background should be considered when deriving dose-response relationships.

A.   Monitoring and Modeling

The purposes of the monitoring and modeling are not clearly articulated. The purposes need to be stated in the beginning. There are at least three purposes for monitoring: 1) to establish a national rural data network to estimate crop losses from dose-response functions, 2) to determine background concentrations, and 3) to support local ecological effects research. The purposes of the modeling are to calculate ozone concentrations in areas where there are no monitors and to develop ozone reduction strategies.

1.   Establish national rural data network - I think we know enough about the spatial behavior of ozone so that we could design a network now that would cover most croplands. All we need is money. On the other hand, we probably will never be able to afford a network in complex terrain that would provide the same degree of spatial resolution as the network in the croplands.

2.   Monitoring in support of effects research - This would range from merely relating observed damage to ozone concentrations with a single monitor to more sophisticated experimental setups to determine ozone fluxes.

3.   Modeling - We already have regional photochemical grid models that can be used to address both purposes. Probably the weakest link here are the emissions inventories for both anthropogenic and biogenic species. In particular, the biogenic inventories are thought to have an uncertainty of a factor of 3.

Ms. Diana Pozun, Management Assistant, U. S. Environmental Protection Agency, Science Advisory
Board, Washington, DC

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