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MEMORANDUM

SUBJECT: CASAC Review of First External Review Draft Ozone Air Quality Criteria Document

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As part of the Environmental Protection Agency's (EPA) ongoing periodic review of the National Ambient Air Quality Standards (NAAQS) for ozone (O_3), an updated revision of the EPA document entitled*, Air Quality Criteria for Ozone and Related Photochemical Oxidants,* has been prepared by EPA's National Center for Environmental Assessment, Research Triangle Park, NC (NCEA-RTP). The First External Review Draft of that revised Ozone Air Quality Criteria Document (First Draft O_3 AQCD), consisting of three volumes (EPA/600/R-05/004aA-cA*,* January 2005), was made available for public comment by posting on the Agency's NCEA Web Site under "Risk Assessments (Ozone)" at the following URL: http://cfpub.epa.gov/ncea/. In addition, CD-ROM and/or hard copies of that First Draft O_3 AQCD were sent to members of the new Clean Air Scientific Advisory Committee (CASAC) Ozone Review Panel. This First Draft O_3 AQCD is to be the focus of a peer review by that CASAC panel at a public meeting on May 4-5, 2005 in Research Triangle Park, NC.

The purpose of the O_3 AQCD to be reviewed is to provide a critical assessment of the latest available scientific and technical information in peer-reviewed published literature on the health and welfare effects associated with the presence of O_3 and related photochemical oxidants in the ambient air. The O_3 AQCD will be utilized by EPA's Office of Air Quality Planning and Standards (OAQPS) staff to prepare an Ozone Staff Paper entitled, *Review of the National Ambient Air Quality Standards for Ozone: Policy Assessment of Scientific and Technical Information*. The Ozone Staff Paper will evaluate the policy implications of the key studies and scientific information contained in the O_3 AQCD and present OAQPS staff conclusions and recommendations concerning standard-setting options for the EPA Administrator to consider in determining whether to retain or revise the O_3 NAAQS.

An earlier document, *Project Work Plan for Revised Air Quality Criteria for Ozone and Related Photochemical Oxidants* (U.S. EPA, 2002), described the approach to be used in preparation of the subject O_3 AQCD, provided an overview of the planned organizational structure, format, and general contents of the document, and identified a number of key issues to be addressed in the draft O_3 AQCD. That work plan was the subject of a consultation with CASAC in February 2003. Preparation of the subject First Draft O_3 AQCD benefitted both from that 2002 CASAC consultation and from peer-consultative workshop reviews of preliminary draft materials obtained by NCEA/RTP in 2003 and 2004.

The main purpose of this "background and charge memo" is twofold, both: (a) to help orient CASAC Ozone Review Panel reviewers to the overall structure and content of the First Draft O_3 AQCD, and the key issues addressed in it; and (b) to help focus their review on matters of most importance to assist EPA in improving the quality of the document. Accordingly, brief overviews concerning certain key features and issues addressed by the First Draft O_3 AQCD are concisely characterized below, and pertinent charge questions are posed in relation to a number of important topics.

A. Format and Structure of the Draft O_3 AQCD

In developing the January 2005 First Draft O_3 AQCD, NCEA followed past advice from the CASAC to streamline the format of the document to facilitate timely CASAC and public review by focusing more clearly on those issues most relevant to the policy assessment to be provided in the Staff Paper. As described in Chapter 1 of the draft Ozone AQCD, emphasis is placed on interpretative evaluation and integration of evidence in the main body of the document, with more detailed descriptions of individual studies being presented in a series of accompanying annexes. Key information from historical ozone-related literature is only succinctly summarized (usually without citation) in the opening paragraphs of each section or subsection, to provide a very brief overview of previous work. For more detailed discussion of pre-1996 work, readers are referred to EPA's 1996 O_3 AQCD. This revised format is intended to make each chapter a more manageable length, to focus on interpretation and synthesis of relevant new research, and to avoid redundancy with the previous O_3 AQCD. Because this revised format only started to be put into place in later phases of preparation of the First Draft O_3 AQCD, the current draft does not fully embody the revised format, especially in those chapters dealing with welfare effects. EPA intends, following the CASAC review in May 2005, to use the revised format throughout a subsequent draft.

As for overall structure and content, after an introductory chapter (Chapter 1), the First Draft O_3 AQCD presents chapters addressing three main topic areas:

- Characterization of ambient O_3, including the physics and chemistry of O_3 in the atmosphere (Chapter 2) and environmental concentrations, patterns, and exposure estimates of O_3 (Chapter 3);
- O_3-related health effects, including dosimetry and extrapolation (Chapter 4), toxicological effects in animals and in vitro test systems (Chapter 5), controlled human

exposure studies (Chapter 6), epidemiology studies (Chapter 7), and an integrative synthesis of O_3 health effects (Chapter 8); and

- O_3-related welfare effects, including environmental effects on vegetation and ecosystems (Chapter 9), tropospheric O_3 effects on UV-B flux and climate change processes (Chapter 10), and effects of O_3 on man-made materials (Chapter 11).

Charge Question A1. To what extent is the document format restructuring *(i.e.*, main chapters of the draft Ozone AQCD focused on evaluative/interpretive aspects, with descriptive materials presented in annexes) useful and desirable? Can the restructuring be further improved? If so, how?

B. Characterization of Ozone-Related Atmospheric Processes, Measurement Methods, Air Quality Patterns and Exposure

1. Policy Relevant Background (PRB) Ozone. PRB ozone concentrations will ultimately be taken into account by OAQPS in analyses to be included in the Ozone Staff Paper that attempt to estimate risks to human health and environmental effects associated with exposures to ozone concentrations attributable to anthropogenic sources of precursors emitted in the United States, Canada and Mexico (*i.e.*, to ozone levels above PRB concentrations). The estimation of PRB ozone concentrations precludes the use of observational data alone because of substantial production and transport from anthropogenic sources in the United States and bordering countries . Contributions to PRB ozone arise from intrusions of stratospheric ozone, biogenic and other natural sources of ozone precursors, and anthropogenic sources outside of the U.S., Canada and Mexico. The modeling approach that has been adopted for estimation of PRB concentrations is based on peer reviewed journal articles describing the GEOS-CHEM model, its evaluation and application to the calculation of PRB ozone values.

Charge Question B1. Does Chapter 3 appropriately and sufficiently characterize the science supporting the basis for estimates of policy relevant background? In particular, is the approach for determining PRB ozone concentrations outlined in Section 3.7 and in AX3.9 based on the best available methodology?

2. Ozone Spatial and Temporal Variability. The characterization of spatial variability in Chapter 3 follows essentially the same methodology as was used in the latest PM AQCD, which provides information about: (a) the representativeness of community monitors or spatial averaging of monitoring results; and (b) the potential for exposure misclassification in urban areas. The characterization of temporal variability of ozone allows for judgments to be made regarding the timing of potential human exposures. Both spatial and temporal variability aspects are of considerable importance in understanding and interpreting epidemiologic (observational) studies and relating their results to those of human and/or laboratory animal controlled exposure studies.

Charge Question B2. Does the discussion of ground-level O_3 concentrations adequately describe the variability attributed to diurnal patterns, seasonal patterns, and spatial

differences in both urban and non-urban locations? Also, to what extent do the characterizations of temporal and spatial variability of O_3 in urban areas provide support for better understanding and interpreting epidemiologic studies discussed later? How might these characterizations be modified to help enhance such understanding and/or would other characterizations (as time permits) be useful in relation to later evaluation of various welfare effects? Is the summary of the effect of elevation on ozone concentrations sufficient to inform later evaluation of the representativeness of elevated ozone monitors (*e.g.*, rooftop) in relation to ozone levels in the breathing zones in children?

3. Ozone Exposures in Various Microenvironments. An extremely important element of analysis to be included in the OAQPS Ozone Staff Paper is the characterization of factors affecting human exposures to ambient ozone. Such analyses will include: (a) estimation of typical ranges of ambient ozone encountered in different important microenvironments (*e.g.*, outdoors, indoors while in motor vehicles, or indoors while at work or in home residence); (b) delineation of time/activity patterns that assist in estimating patterns of movements between the different classes of microenvironments by various population groups; and, hence, (c) estimation of likely periods of exposure of various potentially susceptible groups (*e.g.*, highly-active healthy children, asthmatic children) to different ambient ozone levels typically encountered in the selected microenvironments.

Charge Question B3. Does Chapter 3 provide a sufficiently discussion of concepts and issues related to human exposures, applicable microenvironments, and modeling of O_3 exposure to serve as a foundation for quantitative exposure analyses to be done in conjunction with the Ozone Staff Paper. How might these discussions be improved?

4. Measurement Methods and Potential Ozone Measurement Bias. Chapter 2 describes measurement methods for ozone and other important oxidant precursor or atmospheric reaction products. Ozone is measured routinely by the UV photometry and chemiluminescence techniques in monitoring networks operated by the EPA, and State and Tribal agencies. Available evidence suggests that there may be small positive interferences in O_3 measurement by the UV photometric technique in some very limited areas, *i.e.*, in areas having high concentrations of products of the oxidation of aromatic hydrocarbons and in situations where there are very high PM concentrations (as in traffic with high PM emitters).

Charge Question B4. H ave the techniques for measuring O_3 and its precursor molecules been adequately described? To what extent do monitoring-related uncertainties raise issues with regard to utilization of the ozone monitoring data, *e.g.*, in estimating potential health risks in epidemiologic analyses?

5. Relationships of Ozone to Other Atmospheric Species. Data for other oxidants such as hydrogen peroxide are sparse and have been obtained only as part of specialized field investigations designed to study atmospheric chemistry. Co-occurrence data is more widely available for the other criteria pollutants.

Charge Question B5. Do the discussions in Section 2.2 discussions on ozone photochemistry and Sections 3.6 and AX3.7 on relationships between ozone and other species reflect well the current state of the science? Do they provide useful background information on "related" oxidants that may be toxic? Does the information given in Sections 3.6 and in AX3.8 on the co-occurrence of ozone with other criteria pollutants usefully inform judgments related to later discussions of epidemiologic analyses? Is the use of threshold values for calculating co-occurrences appropriate?

C. Characterization of Ozone-Related Dosimetry and Health Effects

1. Theoretical Ozone Dosimetry Models. Chapter 4 states that the high degree of consistency in O_3 uptake studies provides increased confidence in the use of theoretical dosimetry models. The chapter further discusses refinements in modeling utilizing advancements in physiological, anatomical, and biochemical data inputs.

Charge Question C1. Does the Panel agree that the newer O_3 dosimetry models better predict respiratory tract distribution and uptake of O_3 and foci of injury from O_3? Are the strengths and weaknesses of the models appropriately characterized? Have any new models been missed that should be included in the discussion?

2. Interspecies Extrapolations. Chapter 4 discusses comparisons between O_3 respiratory tract distribution and uptake in humans with varying demographic characteristics (*e.g.*, age, sex) and health status (*e.g.*, healthy, compromised respiratory health, etc.) and various laboratory animal test species, as well as interspecies similarities and differences in pathophysiological responses to O_3.

Charge Question C2. Is the information in Chapter 4 sufficiently complete in terms of discussion of both qualitative and quantitative extrapolation and of interspecies similarities and differences in O_3 dosimetry and in responses to O_3? Do the relatively high O_3 exposure concentrations/doses used in animals studies and in vitro studies allow valid comparisons to human "real-world" exposure scenarios? New animal uptake studies have not been performed. Thus, the Ozone AQCD is relying on the information presented in the 1996 AQCD which estimated that exercising humans received a 4- to 5-fold higher dose of 0.4 ppm O_3 than resting rats. Does the Panel still consider this a valid comparison? Also, to what extent does the Panel consider evaluations of rodent responses to O_3 as being a valuable tool for predicting human responses to O_3? What about other species (*e.g.*, monkeys) used in laboratory animal studies and the use of resting animals versus exercising humans?

3. Characterization of Short-Term Exposure Effects in Experimental Studies. Chapters 5 and 6 discuss the health effects of short-term O_3 exposures, as delineated by controlled laboratory exposures of human subjects or various laboratory animal species (rodents and primate strains with varying susceptibility to O_3) and *in vitro* systems. For present purposes, it is useful to highlight certain key aspects and to pose charge questions in relation to several main subcategories of types of *in vivo* effects evaluated in those chapters: (a) pulmonary mechanical

function effects (indexed by spirometrically-determined lung function measures, *e.g.*, FEV_1, Sh_{aw}, etc.), respiratory symptoms (indexed by self-reported cough, wheezing, substernal pain, etc.), airway hyperreactivity, or AHR (indexed by pulmonary function response to metacholine or other challenge); (b) inflamation, effects on lung defense mechanisms (*e.g.*, alterations of respiratory tract clearance or immune system components or function) or other injury to lung tissue; (c) cardiovascular effects (indexed by alterations in electrocardiogram readings, thermoregulatory control, etc.); and/or (d) other types of systemic effects (*e.g.*, neurobehavioral).

(a) Acute Pulmonary Function/Respiratory Symptom Effects. Overall, as assessed in Chapter 6, the findings of the relatively few newly available controlled human exposure studies of effects of single or repeated acute exposures (of 1 h or 6-8 h duration) do not appear to provide any basis for altering previous conclusions stated in the 1996 O_3 AQCD with regard to dose-response relationships for short-term O_3 exposure induction of pulmonary function changes (*e.g.*, decreased FEV_1) indicative of acute brochoconstriction in healthy or asthmatic children or adults under light to moderate exercise conditions. The new human exposure studies also verify and extend findings related to attenuation of the acute respiratory function effects after several days of repeated daily O_3 exposures, but tend to indicate less notable increases in respiratory symptoms at lowest acute exposure/exercise levels producing significant pulmonary function decrements. Of much importance are new findings expanding our knowledge of O_3 effects on airway responsiveness in healthy and asthmatic adults and in asthmatic animal models.

Charge Question C3a(i). Have any important new human or laboratory animal controlled exposure studies been missed in Chapter 5 or 6 discussions of short-term O_3 exposure effects on pulmonary function and/or respiratory symptoms? Are the discussions on mouse strains with genetically determined differential susceptibility to O_3 sufficiently clear and useful? Do the chapters adequately discuss newly available controlled exposure studies of airway responsiveness in humans and/or laboratory animal models, and what are CASAC panel views on the discussion of new insights into the mechanisms related to airway hyperreactivity? Are the discussions in both Chapters 5 and 6 (as well as in Chapter 8, Integrative Synthesis) adequate to help characterize the extent to which various O_3-induced pulmonary function/respiratory symptom effects may be considered adverse for various types of exposed human population groups (*i.e.*, as a function of age or respiratory disease status)?

Charge Question C3a(ii). Controlled human and animal exposure studies show that O_3-induced deficits in pulmonary function typically resolve quickly (within a few hours) to baseline when exposure ceases in normal individuals. However, asthmatics can have an extended period (up to 24h) of recovery from lung function decline and airway hyperresponsiveness. To what extent do such findings help to explain the increase in emergency room visits, hospital admissions, and use of asthma medication in asthmatics observed in new epidemiology studies?

(b) Acute Lung Defense/Other Lung Injury Effects. The discussions in Chapters 5 and 6 of the few new studies of short-term O_3 exposure effects on lung clearance and immune system components do not appear to substantially alter key findings and conclusions stated in the 1996 Ozone AQCD concerning such endpoints. However, the newly-available research does notably expand our knowledge about mechanisms underlying O_3-induced lung injury. That is, deleterious health effects of O_3 appear to begin with injury to lung tissue, followed by a cascade of events including inflammation, altered permeability of the epithelial barrier, altered clearance, and (over time) chronic alterations of pulmonary structure. Preexisting respiratory disease may exacerbate of some of these events. New information on the roles of monooxygenases, antioxidants, and alveolar macrophages is discussed in Chapters 5 and 6.

Charge Question C3b(i). Do these discussions, including possible exacerbation of listed effects by preexisting respiratory disease, adequately cover new research in this area?

Charge Question C3b(ii). A large component of Chapter 5 is presentation of data from studies of mice strains with differing genetically-determined sensitivities to O_3. These mouse strains differ in O_3-induced inflammatory responses, lung permeability, and pulmonary responses. NCEA staff consider these studies important as a possible explanation for differing human sensitivities to O_3, though the links between the mouse and human have not yet been established. Does the Panel agree with the inclusion and emphasis placed on this area of research? Do these discussions adequately cover the important new research in this area or were any important studies missed? How might the discussion be improved .

Charge Question C3b(iii). Some preliminary data from acute O_3 exposure animal toxicology and some controlled human exposure studies support epidemiological studies suggesting that asthmatics are a potentially sensitive sub-population. To what extent are the animals models of asthma using rodents sensitized to ovalbumin useful in modeling human asthma? Do these animal models provide useful information in modeling human asthma? To what extent do they provide credible support for the plausibility of the epidemiologic findings?

(c) Cardiovascular Effects. As noted later, there is some lack of consistency among findings from epidemiologic, human exposure and animal controlled studies evaluating possible associations between ambient O_3 exposures and cardiovascular effects in human populations. Also, available controlled human exposure studies have not found any compelling evidence linking O_3 exposure to indicators of altered cardiovascular function. However, some new controlled exposure animal studies have found that short-term exposures to near-ambient O_3 levels can cause certain cardiovascular-related effects (*e.g.* the hypothermic response consisting of decreased core temperature, heart rate, and blood pressure).

Charge Question C3c. Can the panel suggest further inputs that may allow a more complete evaluation of potential cardiovascular effects of O_3?

(d) Other Types of Systemic Effects. There is limited information available from controlled exposure studies on systemic effects in humans or laboratory animals. Most of these short-term exposures used much higher than ambient O_3 concentrations.

Charge Question C3d. Is the existing discussion of such systemic effects adequate? Should it be expanded to take into account any pertinent studies that may have been missed that show such effects at more relevant O_3 exposure levels? Or, alternatively, should this section be dropped entirely as irrelevant for current purposes?

4. Characterization of Long-term Exposure Effects in Controlled Exposure Studies. Chapter 5 also discusses results of controlled human and animal exposure studies that help to elucidate the effects of long-term O_3 exposures, including extended periods of months or years of regularly repeated 1, 4, or 6-8 h per day exposures, continuous low level, or other long-term exposure patterns. The effects of such exposures have been evaluated in animals using various endpoints, *e.g.*, chronic alterations to lung structure or function. No comparable data are available from controlled human exposures.

Charge Question C4a. The issue of differing health risks of continuous versus intermittent daily exposure is discussed in the Ozone AQCD. A series of studies evaluating the long-term morphological effects of simulated, seasonal O_3 in rhesus monkeys is given considerable emphasis. Does the Panel consider these studies to be important in lending biologic plausibility to the causal relationship observed in epidemiology studies between seasonal O_3 exposure and adverse health effects such as lung function decline? Is the discussion of season-specific O_3 health effect estimates adequate?

Charge Question C4b. The weight of evidence from toxicology studies does not support ambient O_3 as a carcinogen in animal models, but a few epidemiologic studies from Mexico City suggest a link between ambient O_3 exposure and genotoxic effects. The Ozone AQCD attributes this inconsistency to possible interspecies differences in this health point and inadequate exposure characterization. Do the present O_3 AQCD discussions adequately cover the state of knowledge regarding the possible genotoxicity/carcinogenicity of O_3?

5. Observational Studies of Short and Long-Term O_3 Exposure Effects. Chapter 7 discusses methodological issues attendant to the use of epidemiologic approaches to study air pollution effects and assesses evidence derived from observational of associations between both short-term (< 24 h average) and long-term (typically annual average) ambient O_3 exposures and various health endpoints. Such endpoints include mortality and morbidity indicators, *e.g.*, hospital admissions, respiratory-related emergency department (ERD) visits, school absences, respiratory symptoms, pulmonary function decrements, etc.? Important new findings from numerous studies published since the 1996 O_3 AQCD — including, perhaps most notably, new evidence for associations between exposures to ambient O_3 and increased risk not only of asthma-related symptoms and ERD visits but also of premature mortality. Numerous issues are discussed in Chapter 7 with regard to assessing the credibility of newly reported findings being attributable to O_3 acting alone or in combination with other ambient co-pollutants and with

regard to the extent that experimental (controlled exposure) study findings lend support to the plausibility of reported epidemiologic associations being causal.

Charge Question C5a. The Ozone AQCD discussions of observational and field studies mainly focus on studies of potential O_3 effects among the general population, school-aged children, the elderly, asthmatics, and outdoor workers. Do the studies and the document discussions adequately cover the key populations that should be considered? Are discussions of differences in individual vulnerability and susceptibility adequate?

Charge Question C5b. Chapter 7 highlights the evaluation of two large multi-city studies that examined ambient O_3 effects on mortality, *i.e.*, the study of 95 U.S. communities and the study of 23 European cities. These studies show positive and significant O_3 effect estimates for all cause (non-accidental) mortality. Does the discussion of those studies adequately address questions regarding possible confounding by co-occurring PM, *i.e.*, indicating that the O_3 effect on mortality is independent of PM? Also, is the issue of the seasonality of O_3-mortality effects adequately addressed?

Charge Question C5c. The temporal relationship between O_3 exposure and the occurrence of health effects is important in animal toxicology studies, controlled human studies, and epidemiology studies. Most epidemiology studies find an immediate O_3 effect, with health effects having the strongest associations with acute exposure on the same day and/or previous day. What are the views of the Panel on the adequacy of the discussion on choice of lag period between ozone exposure and the observed health effect? Are sensitivity analyses appropriately considered to address model specification for adjustment of potential confounding by temporal trends in epidemiologic studies?

Charge Question C5d. Given our experience during the past several years in dealing with GAM-related statistical issues in the recently issued PM AQCD (October 2005), NCEA staff has generally excluded epidemiology studies using GAM with default convergence criteria from consideration in the current draft O_3 AQCD. Is the CASAC Panel in agreement with this choice?

Charge Question C5e. The O_3 AQCD evaluates the appropriateness of O_3 exposure assessments used in the epidemiological studies. Does the panel consider the discussion of ambient versus personal monitoring and choice of exposure indices to be adequate? How might it be further strengthened?

6. Integrative Synthesis of Exposure, Dosimetry, and Health Effects Information. Chapter 8 of the O_3 AQCD aims to provide an overall interpretive synthesis of the most important and pertinent findings and conclusions derived from the evaluations contained in the earlier chapters, especially with regard to typical levels and patterns of human exposure to ambient O_3 in the United States, dosimetric considerations, and health effects information derived from both human observational and controlled human and laboratory animal studies.

Charge Question C6a. Are the topics chosen for discussion in Chapter 8 appropriate ones and are they sufficiently clearly addressed? Are there any other important topics or issues that need to be added in the Chapter 8 Integrative Synthesis? In particular, NCEA staff consider the following health endpoints associated with short-term exposure to be important in evaluating adverse health outcomes from O_3 exposure: premature mortality, hospital admissions for respiratory illness, emergency department visits for respiratory illness, lung function decrements, and respiratory symptoms. Is this list sufficiently comprehensive or should other health endpoints be considered?

Charge Question C6b. Myriad health effects described in both epidemiology and controlled exposure human and animal studies (including decreased pulmonary function and various respiratory symptoms) are highlighted as being of possible health significance in Chapter 8 and elsewhere. Are the earlier discussions in Chapters 5 and 6 adequate to help characterize the extent to which various O_3-induced pulmonary function/respiratory symptom effects may be considered adverse for various types of exposed human population groups (*i.e.*, as a function of age and respiratory disease status)? How much short-term or reversible impairment is necessary to be considered a "biologically significant adverse effect?" for adults, children or adults with varying severity of asthma, etc.)? Does Table 8-2, brought forward largely intact from the 1996 O_3 AQCD, still accurately characterize mild through severe functional and symptomatic responses? Also, is Table 8-3 still relevant for characterizing gradations of individual responses to short-term O_3 exposure in individuals with impaired respiratory systems?

D. Characterization of Ozone-Related Welfare Effects

1. Methodologies Used in Vegetation Research. Section 9.2 notes that, to date, most data on exposure-response relationships for crop yield and tree growth have been derived from open-top chamber (OTC) studies. However, numerous chamber effects have been documented and the limited ability to extrapolate chamber data to the field, has been recognized. Some recent studies, however, have employed an alternative methodology, the Free Air Control Exposure systems (FACE)[1]. Another method for characterizing exposures in the field is the use of passive monitoring. Additionally, there has been an increasing reliance on air quality models to fill in the gaps in rural and remote U.S. regions where there is inadequate monitoring.

Charge Question D1. Is the discussion of methodologies used in vegetation research sufficiently clear and adequate to allow comparisons between methodologies and to allow characterization of the uncertainties associated with estimating exposures to vegetation with each system? In particular, is the new FACE technology adequately characterized, and to what extent has it overcome the limitations of the OTC method? What are the uncertainties associated with the FACE data that would apply if trying to extrapolate to other regions of the country with different ozone exposure regimes and vegetation growing conditions?

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[1]Recent studies on the effects of ozone on soybean using the FACE methodology will be included in the next draft of the AQCD.

Given that the results from FACE studies are similar to findings from earlier OTC studies, does this increase our confidence in the results from studies using the OTC methodology? Lastly, would it be useful to move Section 9.2 to an Annex?

2. Mode of Action Underlying O_3 Vegetation Effects. Processes involved in ozone uptake and toxicity are better understood today than in 1996, based largely on advances gained through use of molecular techniques in following rapid O_3-induced changes within the leaf, as discussed in Chapter 9, Section 9.3. O_3 entrance into the leaf via stomata is a critical step in sensitivity. Initial O_3 reactions within the leaf remain unclear except for involvement of hydrogen peroxide. Also, reactions of ozone or its products with ascorbate and other antioxidants in the apoplastic space of mesophyll cells serve to lower the amount of O_3 or products available to alter plasma membranes of the cell. A primary trigger of O_3-induced cell responses appears to be changes in internal Ca levels; and the primary set of metabolic reactions triggered by O_3 comprise "wounding" responses like those generated by cutting the leaf or insect attack. Longer-term responses under low concentrations over long time periods, are linked to senescence or some physiological response very closely linked to senescence (*i.e.*, translocation, reallocation, reabsorption of nutrients and carbon).

Charge Question D2. Has any important new information been missed on mode-of-action for O_3-induced vegetation effects? Also, to what extent does the new information on the mode of action of ozone at the cellular, molecular or biochemical level significant alter our understanding of plant effects?

3. Modification of Growth Response. Chapter 9 notes that none of the few new studies since the 1996 review significantly alter our understanding of how other biotic and abiotic factors modify plant response to O_3. As for biotic interactions, new evidence on insect pests and diseases has not reduced uncertainties noted in the 1996 O_3 AQCD; we still cannot predict the nature of any particular O_3-plant-insect interaction, its likelihood or its severity or of O_3-disease interactions. Nor does new evidence improve our understanding of interactions between O_3 and root symbionts. The few new studies of O_3 effects of plant competition suggest that grasses frequently show greater resilience than other types of plants; but there are insufficient bases to predict specific plant competition situations, *e.g.*, successional plant communities or crop-weed interaction. Temperature is an important variable affecting plant response to O_3, but available data quantifying this interaction are limited and often contradictory. Evidence does suggest that O_3 exposure sensitizes plants to low temperatures by reducing important belowground carbohydrate reserves (which impairs grown in the following seasons). Both increased ambient air relative humidity and/or soil water availability appear to enhance plant sensitivity to O_3. Information on O_3 interactions with specific nutrients is still contradictory; but some experimental data suggests that low fertility increases O_3 sensitivity, while model simulations of tree growth suggest nutrient deficiency and O_3 interact less than additively. There is emerging information regarding potential interactions of O_3 exposure and global change factors, including concurrent elevated CO_2, elevated temperature, altered nutrient and water availability, as well as increased surface UV-B radiation. Studies using elevated O_3 in the presence of high CO_2

without elevated temperature are of limited value for assessing impacts of climate change on response to O_3.

> **Charge Question D3**. Was any important pertinent information missed in the Chapter 9 discussions of factors that modify plant growth response to O_3 exposure? Also, is there sufficient information in the literature and has it been discussed adequately to predict how elevated CO_2, temperature, drought and/or other climate change factors may modify plant response to ozone?

4. Exposure Indices. One of the most important continuing challenges faced in the 1996 O_3 AQCD — and again addressed in Chapter 9 of the current draft Ozone AQCD — is how to incorporate plant biology and interacting physical, site, and meteorological processes into air quality indices reflective of exposure- or dose-response relationships for O_3-induced vegetation effects. The few pertinent new studies since 1996 appear to substantiate earlier conclusions on the role of exposure components (*e.g.*, concentration, duration, and seasonal exposure patterns) in determining effects of O_3 on plant growth responses; and ambient exposure indices (*e.g.*, SUM06) continue to be seen by some as good surrogates for actual O_3 exposures affecting plant target tissues. New studies also demonstrate potential disconnects between peak O_3 events and maximal stomatal conductance periods, either due to site and meteorological factors or day/night differences in conductance. The lack of coincidence in temporal patterns of conductance and peak concentrations introduces uncertainty into regional and national scale assessments because of climate and site factors that modify response to O_3. A large amount of literature regarding a flux-based approach, in contrast to the ambient exposure approach for an index, is bolstered by much progress in developing and testing stomatal models that may be generally applicable across certain vegetation types and landscapes.

> **Charge Question D4.** Are there ways that the Chapter 9 discussion of exposure indices can be improved. For example, are there any published data not appropriately considered in the Chapter 9 discussions? To what extent are the conclusions from this section consistent with our current capabilities to address spatial and temporal factors in exposure and effects on plants? Are there new experimental data that would call into question the conclusions of 1996 that a best available exposure index is one that cumulates hourly concentrations over a three-month period and weights concentration and daylight hours? Are there sufficient data on the relationship between ozone flux and plant response to move away from an ambient exposure-based approach to developing an index at this time? Also, are there adequate experimental exposure-response data for relevant crop species, annual and perennial plants species, and tree species as seedlings to support Chapter 9 conclusions regarding concentration levels of an exposure index that is protective of vegetation?

5. Exposure-Response Relationships for Individual Plant species. Newly available information supports the 1996 O_3 AQCD conclusions that ambient O_3 concentrations are reducing the yield of major crops. New FACE studies support findings from earlier open-top chamber studies of deciduous tree species and crop species. New studies support earlier generalizations: woody plants (*i.e.*, seedling tree species) are less sensitive than are most annual plant species (including

agronomic crops), with the exception of a few deciduous tree species. Current ambient O_3 concentrations in the U.S. are sufficient to reduce growth in seedlings of these sensitive species. Coniferous species are generally less sensitive than most deciduous species in the U.S., and slow-growing species are less sensitive than fast-growing ones. Long-lived species present difficult problems in assessing O_3 impacts, because even multiple-year exposures do not expose trees to O_3 for more than a small fraction of their lives and because competition may exacerbate O_3 effects on individuals (thus making it difficult to determine effects on mature trees).

> **Charge Question D5.** Does the discussion in Chapter 9 of exposure-response relationships for O_3 effects on individual types of plants accurately and adequately characterize the most pertinent available information on the subject? Was any important relevant information missed? How might the discussion be improved? Are multiple species mixes and/or multi-year studies adequately covered? Also, are there adequate experimental exposure-response data for relevant crop species, annual and perennial plant species, and tree species as seedlings to support conclusions regarding concentration levels that might be judged to be protective of vegetation?

6. Ecosystem Response. Despite growing recognition of possible O_3 ecosystem effects, the database demonstrating and quantifying the degree to which O_3 is altering natural ecosystems is very limited, as discussed in Chapter 9. Much of the impact is speculative and based on several case studies of forest plot field-based data reporting on a number of different species. Little is known about O_3 effects on water, carbon and nutrient cycling, especially at the stand and community levels; and little is known about O_3 effects on structural or functional components of soil food webs or how these impacts may affect plant species diversity. Also, little is known about feedbacks between O_3 exposures and climate change effects on ecosystem productivity, given the lack of interaction studies with other components of climate change (*e.g.*, warming, water availability, N deposition). Most of the available data is from seedling studies and annual plants, thus limiting use of these data in developing an understanding of O_3 impacts on natural ecosystems and services derived from them. In general, methodologies to determine the important services and benefits derived from natural ecosystems are lacking, making it difficult to identify and quantify factors that could be used in quantitatively assessing O_3 -related ecosystem effects.

> **Charge Question D6.** How can the Chapter 9 assessment of existing literature on ecosystem response to O_3 be improved? Is the information discussed sufficient to evaluate whether current air quality is damaging natural or managed ecosystems? For example, does new information regarding the role of N in the San Bernardino forests alter our previous understanding of how O_3 affects the ponderosa pine ecosystem? Was any new information missed by which to identify other useful endpoints or measures for assessing ecosystem response to O_3? Also, are there appropriate measures of ecosystem services supported by published literature that would provide better linkages to economic or societal valuation of these services? Is the discussion of ecosystem services adequate for the available information at this time?

7. UV-B Flux and Climate Change. Chapter 10 provides a concise overview of key information regarding tropospheric O_3 effects on UV-B flux at the earth's surface. It also briefly discusses factors governing human exposures to ultraviolet radiation and potential impacts on human health (both deleterious and possibly beneficial effects) that may result from such exposure. In addition, the chapter discusses the role of tropospheric O_3 in climate change processes, including both direct and indirect climate forcing due to O_3. Overall, the chapter concludes that, due to a variety of factors, quantification of tropospheric O_3 effects on surface-level UV-B flux or to climate change processes (as well as consequent contributions to health or welfare effects) would be highly uncertain at this time.

> **Charge Question D7.** What are the views of the Panel on the adequacy and clarity of the presentation of the evidence on the role of tropospheric ozone in ground-level UV-B flux and UV-related health and environmental effects? In general, have the factors governing UV radiation flux at the earth's surface and human exposure to UV radiation been appropriately addressed? In particular, is the discussion of the influence of ozone on ground-level UV radiation flux adequate? Are potential human health impacts due to UV radiation addressed adequately for present purposes? In particular, has the possibility of UV-related deleterious or beneficial health effects from changes in tropospheric ozone levels been suitably discussed? What are the views of the Panel on the scientific soundness and usefulness of the discussion in Chapter 10 of O_3 interactions with global climate change components, *e.g.*, increased atmospheric CO_2, increased mean global temperatures?

We look forward to discussing the above-noted issues with the CASAC O_3 Panel at the upcoming May 4-5, 2005 public meeting. Should you have any questions regarding the first external review draft O_3 AQCD, please feel free to contact me at phone: 919-541-4173, or e-mail: grant.lester@epa.gov; or, please contact Dr. Lori White at phone: 919-541-3146 or e-mail: white.lori@epa.gov.