



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
NATIONAL CENTER FOR ENVIRONMENTAL ASSESSMENT  
RESEARCH TRIANGLE PARK, NC 27711

OFFICE OF  
RESEARCH AND DEVELOPMENT

July 18, 2012

**MEMORANDUM**

**SUBJECT:** CASAC Review of Third External Review Draft Integrated Science Assessment for Ozone and Related Photochemical Oxidants

**FROM:** John Vandenberg, Ph.D.  
Director  
National Center for Environmental Assessment  
Research Triangle Park Division (B243-01)

**TO:** Holly Stallworth, Ph.D.  
Designated Federal Officer  
Clean Air Scientific Advisory Committee  
EPA Science Advisory Board Staff Office (1400R)

The *Third External Review Draft Integrated Science Assessment for Ozone and Related Photochemical Oxidants* (draft O<sub>3</sub> ISA) prepared by the Environmental Protection Agency's (EPA) National Center for Environmental Assessment – Research Triangle Park Division (NCEA –RTP) as part of EPA's ongoing review of the national ambient air quality standards (NAAQS) for ozone (O<sub>3</sub>) was released on June 15, 2012. This third external review draft ISA integrates the scientific evidence for review of the primary (health-based) and secondary (welfare-based) NAAQS for O<sub>3</sub> and provides draft findings, conclusions and judgments on the strength, coherence and plausibility of the evidence. The ISA is intended to “accurately reflect the latest scientific knowledge useful in indicating the kind and extent of identifiable effects on public health which may be expected from the presence of [a] pollutant in ambient air” (Clean Air Act, Section 108; 42 U.S.C. 7408). The draft ISA will be reviewed by the Clean Air Scientific Advisory Committee (CASAC) O<sub>3</sub> NAAQS Review Panel (the O<sub>3</sub> CASAC Panel) at a public meeting on September 11-13, 2012. We have distributed the draft O<sub>3</sub> ISA to the O<sub>3</sub> CASAC Panel. I am requesting that you forward our charge to the O<sub>3</sub> CASAC Panel.

Following the review of the third external review draft ISA, NCEA-RTP staff will produce a final O<sub>3</sub> ISA projected for release in December 2012 that addresses comments received from the CASAC O<sub>3</sub> Panel and the public. The final O<sub>3</sub> ISA, in conjunction with additional technical assessments, will provide the scientific basis for EPA's decision regarding the adequacy of the current standards for O<sub>3</sub> to protect human health, public welfare, and the environment.

We look forward to the O<sub>3</sub> CASAC Panel review of the third draft ISA at the upcoming meeting. Should you have any questions regarding the draft O<sub>3</sub> ISA, please feel free to contact Dr. Mary Ross (919-541-5170, [Ross.Mary@epa.gov](mailto:Ross.Mary@epa.gov)) or Dr. James Brown (919-541-0765, [Brown.James@epa.gov](mailto:Brown.James@epa.gov)).

### **Charge to the O<sub>3</sub> CASAC Panel**

This draft ISA includes revisions based on the comments and advice provided by the CASAC O<sub>3</sub> Panel and public comments on the second external review draft ISA. Specific revisions to the third draft O<sub>3</sub> ISA were described in more detail in EPA's recent response (May 22, 2012) to the CASAC O<sub>3</sub> Panel's review letter (March 13, 2012) on the second draft Ozone ISA. We have carefully considered all of the comments provided by the CASAC O<sub>3</sub> Panel members and the public in creating this third draft ISA. In particular, we focused on several key overarching points raised by the CASAC Panel:

- integration of evidence across scientific disciplines;
- causal determination for short-term O<sub>3</sub> exposure and cardiovascular effects;
- characterization of potentially at-risk populations; and
- discussion of background ozone concentrations.

Changes to the content and structure of the draft ISA are highlighted below together with the new charge questions for this CASAC O<sub>3</sub> Panel review. These charge questions are not intended to limit the scope of the Panel's review, rather these charge questions are intended to assist the Panel by highlighting specific areas where the Agency has responded to prior comments of the Panel or where the Agency raises emerging issues to the attention of the Panel for comment.

### **Preamble; Legislative and Historical Background (formally Preface)**

The CASAC Panel recommended flow diagrams be included in the Preamble for clarity of presentation. In the Preface, the Panel noted several omissions in the recent history and recommended updating the history to include recent decisions. The Panel also recommended renaming the Preface to reflect its historical content. Several diagrams were added to the Preamble to more effectively and clearly communicate the process of ISA development and the NAAQS review process. The Preface was renamed to reflect its content and revised to include a more complete and up-to-date history of activities.

Please review and comment on the effectiveness of these revisions. Please comment on the extent to which these sections of the ISA provide a useful and effective format for presenting introductory materials for this and future ISAs. Please recommend any revisions that may further improve the clarity of discussion.

### **Chapters 1 (Executive Summary) and 2 (Integrative Overview)**

In response to CASAC comments, the language in Chapter 1 was simplified and figures were removed to improve the readability for a non-technical audience. Call-outs were added to Chapters 1 and 2 for ease of accessing more detailed discussions in the rest of the ISA. Both chapters were updated to reflect revisions in subsequent chapters. In Chapter 2, relative to the last draft of the chapter, there is increased integration of health effects evidence across scientific disciplines and health endpoints. Discussion of heterogeneity in risk estimates was expanded and synthesized.

Please comment on the adequacy of these and other changes to the chapters and recommend any revisions to improve the discussion of key information. Please recommend any revisions that may further improve the clarity of discussion.

### **Chapter 3 – Atmospheric Chemistry and Ambient Concentrations**

In revising Chapter 3, particular attention was given to estimates of background O<sub>3</sub> concentrations. At the request of CASAC, new studies published after completion of the prior draft were evaluated and added to the discussion in Section 3.4. There is also increased focus on background estimates relevant to the fourth-highest maximum daily 8-hour average O<sub>3</sub> concentrations.

Please comment on the adequacy of these and other changes to the chapter and recommend any revisions to improve the discussion of key information. In relation to ambient and background O<sub>3</sub> concentrations, is material clearly, succinctly, and accurately provided? Where appropriate, please provide guidance that may refine the scientific interpretation and/or improve the representation of the science.

### **Chapter 4 – Exposure to Ambient Ozone**

Revisions made to Chapter 4 in response to CASAC comments included: adding maps that integrate population density, placement of ozone monitors, and concentrations at the monitors; a discussion of long-term concentration averages typically used as exposure metrics in epidemiologic studies; and adding time activity information. These revisions more closely link the information in Chapter 4 with subsequent health information in Chapters 5-8.

Please comment on the adequacy of these and other changes in responding to the Panel's comments. Please provide comment on revisions that may further improve the utility of this chapter for interpretation of epidemiologic results in subsequent chapters.

### **Chapter 5 – Dosimetry and Mode of Action**

Chapter 5 was updated considerably in response to CASAC comments with revisions including expanded characterization of the potential for O<sub>3</sub> reaction products versus O<sub>3</sub> itself to elicit observed health effects, attention to specific exercise levels utilized in the human studies, and enhanced discussion of species homology and interspecies sensitivity.

Please comment on the extent to which these revisions help to provide the underlying mechanistic and dosimetric information for interpretation of health effects evidence in later chapters and recommend any revisions to improve the discussion of key information.

### **Chapters 6-7 – Integrated Health Effects of Short- and Long-Term Ozone Exposure**

Revisions made to Chapters 6 and 7 included increased integration of recent evidence with key findings from previous reviews, and further integration across chapters, particularly with information from Chapters 4 and 8. One key example of further integration across chapters is the expanded discussion of exposure assessment methods and measurement error issues with linkages to Chapter 4 and discussion of their potential influence on heterogeneity of results among studies.

Careful consideration was given to a CASAC recommendation that the causal determination for cardiovascular effects from short-term O<sub>3</sub> exposure be increased to “likely to be a causal relationship.” There was strong toxicological evidence and consistent, positive associations

between short-term O<sub>3</sub> exposure and cardiovascular mortality in epidemiologic studies. However, controlled human exposure studies were limited in number and provided inconsistent results. Likewise, epidemiologic studies showed inconsistent findings for cardiovascular morbidity (e.g., heart rhythm, physiological biomarkers, and hospital admissions or emergency department visits). Based on extensive review and discussion of the evidence the decision was made to retain the “suggestive of a causal relationship” conclusion for cardiovascular effects from short-term O<sub>3</sub> exposure.

Please comment on the extent to which there is sufficient clarity in the revised presentation of study designs and results. Please provide recommendations where the interpretation of the scientific evidence may be improved as well as comments on the soundness of conclusions in these chapters.

### **Chapter 8 – Populations Potentially at Increased Risk for Ozone-Related Health Effects**

The CASAC encouraged the development of standard terminology and concepts for assessing populations at risk that could be applied broadly across the NAAQS pollutants. To help synthesize the evidence, a new classification system was created for considering risk factors. Similar to the approach used to determine causality, each factor was evaluated and classified based on the weight of evidence within and across disciplines. Throughout the chapter, effort was also made to distinguish between greater ambient exposure and/or greater internal dose versus greater adverse health effects at a specific dose when describing the evidence that could potentially result in a population being at increased risk of an O<sub>3</sub>-related health effect.

Please comment on the adequacy of these revisions to clarify the consideration of potential at-risk populations and recommend any revisions to improve the characterization of key findings and scientific conclusions.

### **Chapter 9 – Environmental Effects: Ozone Effects on Vegetation and Ecosystems;**

### **Chapter 10 – The Role of Tropospheric Ozone in Climate Change and UV-B Effects**

The CASAC Panel provided a number of important comments that led to focused revisions of these chapters. In Chapter 9, clarifying statements were added related the effect of O<sub>3</sub> on root growth. In Chapter 10, a description of the RCP scenarios from the IPCC Fifth Assessment Report was added. Additionally, the discussion of radiative forcing from O<sub>3</sub> precursor emissions was expanded. The discussion in Chapter 10 of tropospheric O<sub>3</sub> health and welfare effects related to UV-B shielding was revised to be more concise with clear conclusions. At the end of both Chapter 9 and 10, a table of causal determinations was added at the request of CASAC.

Please comment on the revisions to these chapters and the adequacy, scientific soundness, and usefulness of the material presented and recommend any revisions to improve the discussion of key information.

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