



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

MAY 22 2012

THE ADMINISTRATOR

Jonathan M. Samet, M.D.
Chairman
Clean Air Scientific Advisory Committee
Science Advisory Board
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Dear Dr. Samet:

Thank you for your March 13, 2012, letter in which you provided the Clean Air Scientific Advisory Committee Ozone Review Panel's comments on the U.S. Environmental Protection Agency's *Integrated Science Assessment for Ozone and Related Photochemical Oxidants, Second External Review Draft – September 2011*. We at the EPA greatly appreciate the panel's thorough review and constructive contributions.

My staff is carefully considering your comments and recommendations as well as the comments we received from the public. We are making revisions to address both the panel's consensus responses and individual comments. Enclosed is an overview of the major revisions being incorporated into the *Third External Review Draft of the ISA for Ozone*.

In responding to the CASAC's comments, we are paying particular attention to several important points the panel raised: the need for increased synthesis and integration of the scientific evidence; the need for revisions to the discussion of background ozone concentrations; the need to consider revisions to the causal determination for short-term cardiovascular effects from ozone exposures; and additional clarifications regarding the populations potentially at greater risk for ozone-related health effects.

The CASAC panel also expressed a need for increased synthesis and integration of scientific evidence across disciplines in the integrative overview in chapter 2 and in subsequent health chapters 5-8. The third external review draft will also address this need. For instance, there will be more consideration of personal-ambient exposure relationships carried from chapter 4 into chapters 6 and 7 in relation to the interpretation of epidemiologic studies. Discussion of activity levels in the general population and in experimental studies is being added to chapters 4, 5, 6 and 8.

Additionally, the third external review draft will address comments from both the CASAC panel and the public about the need to revise discussions of background ozone concentrations in chapter 3 to better inform policy documents. Specifically, we are adding discussion that focuses on background estimates relevant to the annual fourth-highest maximum daily eight-hour average ozone concentrations. The discussion will better describe model limitations in relation to predicting high extremes and to

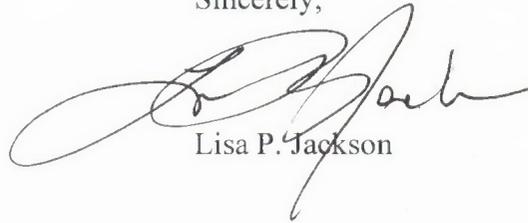
emphasize clear differences in the western mountains from other regions of the nation. Further, we are revising and expanding the discussion of the utility and uncertainty in satellite observations.

The CASAC panel recommended that the EPA consider revising the causal determination for short-term cardiovascular effects from “suggestive of a causal relationship” to “likely to be causal relationship.” The EPA is thoroughly considering the weight of evidence for the causal determination for short-term ozone exposure and cardiovascular effects to clearly articulate the scientific basis as it relates to the EPA’s framework for causal determinations. At this time, EPA staff is still evaluating the evidence, and the third external review draft will present the rationale for our conclusion in the causal determination summary in section 6.3 of the ISA.

The CASAC panel also offered advice on characterizing populations potentially at risk for ozone-related health effects. Chapter 8 is being modified to clearly distinguish two broad processes that can affect risk: a greater ozone exposure or dose and a greater magnitude of health effects at a specific dose. The staff is also considering strategies to improve the synthesis and characterization of the weight of evidence for the evaluation of groups potentially at risk for ozone-related health effects.

We recognize that our efforts to protect the environment can only be as good as the science upon which it is based. Your independent critical reviews help to ensure that we use the best science to protect our nation’s environment. Please accept my appreciation for your hard work and thoughtful review.

Sincerely,

A handwritten signature in black ink, appearing to read "Lisa P. Jackson", with a large, sweeping flourish extending to the left.

Lisa P. Jackson

Enclosure

ATTACHMENT

Overview of Revisions to the Second Draft Ozone ISA in Response to CASAC Peer Review Comments dated March 13, 2012

Preface

Within the historical discussion of the National Ambient Air Quality Standard (NAAQS) for O₃, the preface is being revised to include a more complete and up to date history of activities.

Chapter 1 – Executive Summary

The language is being simplified for a non-technical audience. Call-outs to subsequent chapters will be included to make it easier to locate more detailed discussions. Overly-technical or confusing figures are being removed.

Chapter 2 – Integrative Summary

This chapter is being revised to include additional synthesis and integration, especially across health effects and scientific disciplines, and to more thoroughly integrate exposure assessment into the discussion of the health effects evidence. Figure 2-3 (pyramid/triangle respiratory effects) is being deleted. Table 2-1 is being updated and reformatted to include more detail and aid in its interpretation.

Other major changes will include the addition of a summary and conclusion paragraph to the end of each section in this chapter, and a more focused and concise discussion of tropospheric ozone and UV-B related effects.

Chapter 3 – Atmospheric Chemistry and Ambient Concentrations

Section 3.2

The discussion of chemistry in western oil and gas fields is being expanded. A discussion of the utility and uncertainty in satellite observations is being expanded and revised.

Section 3.4

The results from three important new studies addressing background O₃ concentrations are being added and evaluated as requested by CASAC. The results presented in one of the studies (Emery et al.) are being evaluated to obtain a more meaningful comparison with GEOS-Chem results. Information is being added to focus on background estimates relevant to the fourth-highest maximum daily 8-hour average O₃ concentrations. Additional comparisons between model simulations and observations are being added.

Section 3.6

An updated and expanded analysis of O₃ trends was included.

Section 3.9

This section on O₃ background modeling using GEOS-Chem (v9-01-01) is being deleted.

Chapter 4 – Exposure to Ambient Ozone

A discussion of long-term concentration averages typically used as exposure metrics in epidemiologic studies is being added. Section 4.5.3, which described previous NAAQS scenario exposure simulations, is being removed from the chapter. Maps showing population density, placement of ozone monitors and concentrations at the monitors are being added to support a discussion of monitor representativeness and population proximity to monitors.

Integration of exposure information with materials presented in Chapters 3 and 5-8 is being improved, particularly regarding: ozone concentrations and trends; exposure estimation methods in epidemiologic studies; and age-related differences in time spent outdoors, exertion level and activity pattern.

Chapter 5 – Dosimetry and Mode of Action

Chapter revisions are being made related to: (1) characterization of the potential for O₃ or O₃ reaction products to be responsible for effects observed with O₃ exposure, (2) clarification of the dose distribution that relates to tissue damage, and (3) enhanced discussion on species homology and interspecies sensitivity. In addition, Chapter 5 is being better integrated within the chapter and with the other chapters.

Section 5.2

To improve ease of reading, definitions will be provided for the various dose metrics used in the chapter. These definitions will be consistently applied throughout Chapters 4-7. A table of general adult human inhalation rates by activity levels is being added to Section 5.2.2.7 and the new tables on exercise levels in Chapters 4 and 6 are being referenced.

Section 5.3

Revisions being made in response to CASAC comments include: providing additional information on experimental protocols such as the exercise levels employed, clarifying whether mode(s) of action are related to direct reactions of ozone with cells or with ELF components, and expanding the discussion of the mechanisms by which ozone impacts development.

Chapter 6 – Integrative Health Effects of Short-term Ozone Exposure

Throughout the chapter, for consistency, studies published since the completion of the previous AQCD are being referred to as “recent” studies. Key studies from previous reviews are being integrated with the more recent evidence to further build on the total body of evidence for health effects due to short-term O₃ exposures. To put the recent studies in the appropriate context, the EPA will clarify whether these recent studies make a critical advance in the strength of the overall evidence. Additionally, a consistent standardization approach will be used throughout the chapter when presenting effect estimates from epidemiologic studies. A description of the standardization approach is being added to Section 2.2. Overall, when discussing the epidemiologic evidence, study-specific details regarding exposure assessment will be added. Linkages are also being made with Chapter 4 to more fully address some of the exposure measurement error issues raised in epidemiologic studies.

Section 6.2

Additional details are being added to more accurately describe exercise conditions used in human clinical studies. Activity levels, originally described only in terms of ventilation rates, will now also be described in terms of heart rate and treadmill walking speeds for ease of interpretation. Consideration of O₃ exposures producing changes in both lung function and respiratory symptoms are being expanded to improve the linkage to adversity of effects. The discussion of O₃-associated respiratory symptoms and medication use in children with asthma describes evidence from two recent multi-city studies as weak. In the context of a large body of high-quality, single-city or single-region studies, the EPA concludes that the weight of cumulative evidence continues to support associations between short-term ambient ozone exposure and respiratory symptoms and medication use in children with asthma. The EPA is refining the text to further describe the scientific support that underlies this conclusion.

Section 6.3

The EPA is thoroughly considering the weight of evidence for the causal determination for short-term O₃ exposure and cardiovascular effects to clearly articulate the scientific basis as it relates to the EPA's framework for causal determinations. At this time, the staff is still evaluating the evidence and the third draft will present the rationale for our conclusion in the causal determination summary in Section 6.3 of the ISA.

Section 6.6

The summary of the evidence for short-term O₃ exposure and mortality is being edited to clearly articulate the lines of evidence that contribute to the causal determination, including studies that examined cause-specific mortality. Additionally, the discussion has been modified to emphasize that the causal determination is made for all-cause mortality, and not each individual cause-specific mortality outcome.

Chapter 7 – Integrative Health Effects of Long-term Ozone Exposure

Efforts are being made to more clearly distinguish between long-term and short-term exposures in the text. The EPA is carefully considering CASAC's suggestion to move the results of studies of short-term exposure and reproductive or developmental effects to Chapter 6. Due to the length of gestation, however, an epidemiologic study using the entire pregnancy as the exposure period is considered a long-term exposure (about 40 weeks), whereas, a toxicological of rats also using the entire pregnancy is a short-term exposure (about 18-24 days). After much deliberation, the EPA presently anticipates that maintaining the results of all studies in one section will facilitate characterization of the weight of evidence for the effects of O₃ on reproductive and developmental effects in a consistent, cohesive and integrated manner. This approach will be discussed at the beginning of Chapter 7 and in the introduction to the section on Reproductive and Developmental Effects.

Chapter 8 – Populations Potentially at Increased Risk for Ozone-related Health Effects

Throughout the chapter, effort is being made to distinguish between greater ambient exposure and/or greater internal dose versus greater adverse health effects given a specific dose when describing the evidence that could potentially result in a population being at increased risk of an O₃-related health effect. To help synthesize the evidence, a new classification system has been created for the at-risk factors considered. Similar to the approach used to determine causality, each factor will be evaluated and classified based on the weight of evidence within and across disciplines. The new classification system will be explained in detail in the introduction of the chapter and applied to each factor in each section and in the summary of the chapter. Finally, the summary section of the chapter will address limitations inherent in many studies of effect measure modification and how this may affect interpretation of the results.

Chapter 9 – Environmental Effects: Ozone Effects on Vegetation and Ecosystems

A table of causal determinations is being added to the end of the chapter. Statements regarding the effect of ozone on root growth are being clarified. Figures and discussions will be modified to account for a potential decrease as well as potential increase in water loss from plants due to sluggish stomata. The use of "scale" is being checked throughout the chapter and will be clarified where appropriate, and definitions and explanations of terms are being added to the chapter.

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

Section 10.2

A description of the RCP scenarios from the IPCC Fifth Assessment Report is being added. Additionally, the discussion on radiative forcing from O₃ precursor emissions is being expanded.

Section 10.3

The discussion of UV-B health and ecological impact studies previously included in the 2006 O₃ AQCD will be removed, and this section is being revised to make the discussion more concise with clear conclusions.