



**E. SCOTT PRUITT**  
**ADMINISTRATOR**

August 16, 2017

Ana V. Diez Roux, M.D., Ph.D., M.P.H.  
Chair, Clean Air Scientific Advisory Committee  
Science Advisory Board  
U.S. Environmental Protection Agency  
1200 Pennsylvania Avenue, NW  
Washington, D.C. 20460

Dear Dr. Diez Roux:

Thank you for your June 30, 2017, letter providing consensus comments from the Clean Air Scientific Advisory Committee and individual comments from the CASAC Sulfur Oxides Review Panel on the U.S. Environmental Protection Agency's *Integrated Science Assessment for Sulfur Oxides – Health Criteria (Second External Review Draft – December 2016)*. We greatly appreciate the panel's thorough review and constructive comments.

My staff is carefully considering your comments and recommendations as well as the comments we received from the public. We appreciate the very positive comments from CASAC regarding the characterization of the health effects of SO<sub>2</sub> and CASAC's concurrence with the causality determinations presented in the second draft ISA. We are making revisions to address both consensus and individual CASAC comments. Enclosed is an overview of the major revisions we are incorporating into the *ISA for Sulfur Oxides – Health Criteria (Final Report)*. Some of the key changes we are making in response to the CASAC's comments are highlighted below.

We are paying particular attention to several important points raised by the CASAC panel, including:

- revision of the Executive Summary and Integrated Synthesis chapter to clarify and better highlight important information provided in subsequent chapters;
- expansion of cross-referencing across chapters throughout the ISA to ensure that the ISA provides support for topics to be included in the *Risk and Exposure Assessment* and in the *Policy Assessment* prepared by the Office of Air and Radiation;
- updates to information on sources and emissions of sulfur oxides, including contributions of emissions from smelters and integrated iron and steel mills, as well as updating information on spatial and temporal variation in sulfur dioxide concentrations;

- acknowledgment that the American Meteorological Society/Environmental Protection Agency Regulatory Model (AERMOD) can be used to calculate five-minute average SO<sub>2</sub> concentrations;
- revision of the discussion of exposure assessment to improve clarity, language, consistency, organization and readability and to leverage discussions of exposure assessment and exposure modeling from recent ISAs;
- revision of the exposure modeling section to clarify the different approaches to exposure modeling and how selection and application of exposure models influence analyses and conclusions for both epidemiologic studies and risk assessment;
- more effective presentation of the health-effects evidence supporting the causal determinations, including revisions to address panelists' individual comments regarding the chapters on dosimetry and mode of action and health effects of SO<sub>2</sub>; and
- expansion of the introduction to the chapter on at-risk populations and life stages to clarify the objectives of the chapter and the specific factors considered regarding the potential for increased risk for health effects related to sulfur dioxide exposure.

To address the CASAC panel's recommendations for improving the Executive Summary and the Integrated Synthesis chapter, we are clarifying and simplifying the language in certain places, revising the discussion to clarify the rationale for the causality determination for respiratory effects related to long-term SO<sub>2</sub> exposure and more explicitly characterizing the potential for occurrence of high five-minute SO<sub>2</sub> concentrations.

In the chapter on atmospheric sciences, we are updating emissions estimates with more recent information and further characterizing the possible influence of nearby industrial sources on monitors with high SO<sub>2</sub> concentrations, including smelters and other metals processing facilities. The chemistry and formation of other particulate sulfur compounds will be discussed. The environmental concentration data will be reanalyzed with the inclusion of negative values within the instrument's detection limit, and additional interpretation of the results will be provided as recommended by CASAC. The modeling discussion will clarify that other averaging times, including five-minute averages, can be estimated by AERMOD and that biases in model output can lead to biases in model-based health studies.

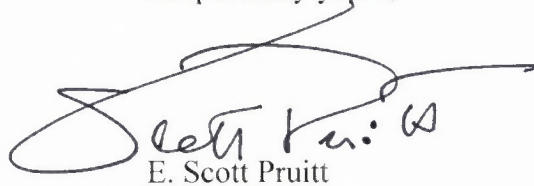
The chapter on exposure to ambient SO<sub>2</sub> will be revised to compare characteristics of exposure assessment and exposure modeling approaches and their application for epidemiologic studies and risk assessment. Material on infiltration, activity tracking and micro-environmental monitoring of SO<sub>2</sub> will be updated. As with the rest of the document, cross-referencing will be expanded and the chapter will be reviewed to ensure topics relevant for the Risk and Exposure Assessment and Policy Assessment are covered appropriately.

We appreciate CASAC's very positive comments on the characterization of the health effects evidence in the ISA, especially regarding the causal relationship between respiratory effects and short-term SO<sub>2</sub> exposure, as well as the causality determinations for the other classes of health outcomes. We are pleased that the revisions made for the second draft ISA address previous CASAC concerns. We are making minor revisions to the chapter on dosimetry and mode of action and to the health chapter in response to CASAC panelists' comments in order to further strengthen these chapters.

We are revising the chapter on characterization of populations and life stages potentially at greater risk of health effects due to SO<sub>2</sub> exposure to more clearly articulate the purpose of the chapter and the approach used to categorize the body of evidence for potential at-risk populations and life stages in accordance with the CASAC panel's advice. We will also clarify that, where SO<sub>2</sub>-specific evidence exists, multiple factors that may combine to increase risk will be considered.

We recognize that our efforts to protect human health and the environment can only be as good as the science upon which they are based. Independent critical reviews like yours help ensure that we use the best science to protect public health and our nation's environment. Please accept my appreciation for your hard work and thoughtful review.

Respectfully yours,



E. Scott Pruitt

Enclosure

## ATTACHMENT

### **Overview of Revisions to the Second Draft Integrated Science Assessment for Sulfur Oxides – Health Criteria in Response to the Clean Air Scientific Advisory Committee Peer Review Comments dated June 30, 2017**

#### **Executive Summary and Chapter 1 – Summary of the Integrated Science Assessment**

Both the Executive Summary and Chapter 1 are being revised to reflect changes made to the subsequent chapters. CASAC has provided some helpful suggestions on places where additional clarifying language would be useful. The discussion of the causality determination for respiratory effects related to long-term SO<sub>2</sub> exposure will be revised to clarify the rationale and highlight the change in causality determination from the 2008 Integrated Science Assessment. The potential for and frequency of occurrence of high five-minute SO<sub>2</sub> concentrations on a national scale will be characterized.

#### **Chapter 2 – Atmospheric Chemistry and Ambient Concentrations of Sulfur Oxides**

Revisions to Chapter 2 are aimed at improving characterization of sources, atmospheric chemistry and fate, environmental concentrations and atmospheric modeling. The chapter is being revised to provide more recent emissions estimates and clarify the contribution from metals processing facilities (e.g. smelters and iron and steel mills) as well as decreasing emissions from motor vehicles. The possible influence of nearby industrial sources on monitors with very high SO<sub>2</sub> concentrations will be further discussed. Material is being added to the atmospheric chemistry section to further discuss the formation of trace inorganic and organic S(IV) and S(VI) species not previously covered, and it will be cross-referenced to a newly added summary of toxicology studies discussed in the previous ISA that evaluated their health effects in combination with SO<sub>2</sub>. The environmental concentration data have been reanalyzed to include negative values within the instrument's noise range to avoid upward bias in summary statistics. The potential for water vapor and noise-reducing time constants to influence SO<sub>2</sub> instrument readings will be elaborated. Additional interpretation of environmental concentration analyses will be provided, including relationships between annual maxima of the national distribution of five-minute hourly maximum and one-hour daily maximum concentrations, the occurrence of very high five-minute concentrations on a national scale and diurnal variations of SO<sub>2</sub> concentrations near large sources. The discussion of peak-to-mean ratios will be clarified to acknowledge the influence of the averaging time of the denominator as well as atmospheric conditions, source type and monitor locations. The modeling discussion will be revised to clarify that five-minute SO<sub>2</sub> concentrations can be estimated by the American Meteorological Society/Environmental Protection Agency Regulatory Model.

#### **Chapter 3 – Exposure to Ambient Sulfur Dioxide**

Chapter 3 will be further refined in several aspects. Definitions, usage and terminology will be clarified based on CASAC comments. Exposure modeling approaches will be compared in terms of their characteristics for use in epidemiologic studies and risk assessment. The introduction to Section 3.4 will be expanded to describe SO<sub>2</sub> epidemiologic study designs that will be discussed

in the section and to clarify the importance of exposure assessment issues for both epidemiologic inference and risk assessment. Material on infiltration, GPS activity tracking and micro-environmental monitoring of SO<sub>2</sub> will be revised and updated. Cross-referencing will be expanded to improve linkages with the atmospheric science and health chapters. The chapter will be reviewed to ensure that key topics supporting risk, exposure and policy assessments will be covered in the ISA.

#### **Chapter 4 – Dosimetry and Mode of Action and Chapter 5 – Integrated Health Effects of Exposure to Sulfur Oxides**

Revisions are being made to Chapter 4 to clarify and focus the discussion of transport, uptake and reactivity of SO<sub>2</sub>. Language was clarified with respect to the reactivity of SO<sub>2</sub> and the impact of acidity on airway physiology. We appreciate CASAC's positive comments on the characterization of the health evidence in Chapter 5 and the panel's support for the causality determinations. Chapter 5 will be revised to clarify language regarding statistical significance and precision and further discuss co-pollutant confounding and its potential influence on epidemiologic study results. Language in Chapter 5 regarding the importance of exercise and elevated ventilation rate, the influence of asthma severity on SO<sub>2</sub> respiratory effects and differing levels of response among individuals with asthma will be reviewed to ensure appropriate emphasis.

#### **Chapter 6 – Populations and Life Stages Potentially at Risk for Health Effects Related to Sulfur Dioxide Exposure**

Chapter 6 is being revised to provide additional details and improve clarity regarding the purpose of the chapter and the approach used to determine the potential for increased risk of SO<sub>2</sub>-related health effects. The discussion of multiple potential at-risk factors will be articulated more clearly.