



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
NATIONAL CENTER FOR ENVIRONMENTAL ASSESSMENT

OFFICE OF
RESEARCH AND DEVELOPMENT

December 2, 2015

MEMORANDUM

SUBJECT: CASAC Review of External Review Draft Integrated Science Assessment for Sulfur Oxides – Health Criteria

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

TO: Aaron Yeow, M.P.H.
Designated Federal Officer
Clean Air Scientific Advisory Committee
U.S. EPA Science Advisory Board Staff Office (1400R)

The *External Review Draft Integrated Science Assessment (ISA) for Sulfur Oxides – Health Criteria (SO_x ISA)* prepared by the U.S. Environmental Protection Agency's (U.S. EPA) National Center for Environmental Assessment – Research Triangle Park Division (NCEA-RTP) as part of the U.S. EPA's ongoing review of the primary (health-based) national ambient air quality standard (NAAQS) for sulfur dioxide (SO₂) was released on November 24, 2015. Electronic copies are available for download at <http://www.epa.gov/isa>. The draft SO_x ISA will be reviewed by the Clean Air Scientific Advisory Committee (CASAC) Augmented for Sulfur Oxides Panel at a public meeting anticipated to be held January 27-28, 2016. I am requesting that you forward our charge to the CASAC Augmented for Sulfur Oxides Panel.

The purpose of the draft SO_x ISA is to identify, evaluate, and summarize scientific information on the health effects associated with gaseous sulfur oxides (SO_x). The SO_x ISA is intended to “accurately reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare, which may be expected from the presence of [a] pollutant in the ambient air” [Clean Air Act, Section 108; 42 U.S.C. 7408(b)]. This external review draft SO_x ISA integrates the scientific evidence for review of the primary (health-based) NAAQS for SO₂ and provides draft findings, conclusions, and judgments on the strength, coherence, and plausibility of the evidence.

As in the final 2008 SO_x ISA, this draft SO_x ISA determines the likelihood of causal relationships only for SO₂; other gaseous sulfur oxide species are not included, as SO₂ is the only gaseous sulfur oxide species present in ambient air at concentrations relevant for public health, and the health effects literature is focused on SO₂. Particulate sulfur oxide species (e.g., sulfate) are considered as part of the review of the NAAQS for particulate matter (PM) (e.g., in the 2009 Integrated Science Assessment for Particulate Matter). The welfare effects of sulfur oxides are being considered in a separate assessment as part of the review of the secondary (welfare-based) NAAQS for oxides of nitrogen and sulfur.

The overall process for ISA development, including criteria used to identify relevant studies, aspects considered in judging the overall weight of evidence, and the framework for causal determination, are described in the Preamble to the Integrated Science Assessments, which is available to the public at NCEA's website (<http://www.epa.gov/isa>) and in the Health and Environmental Research Online (HERO) database ([U.S. EPA, 2015a](#)). The Preamble to the ISA is provided as a companion document to the draft SO_x ISA, and it reflects development and refinements based on peer review and public comment for several prior ISAs [e.g., for ozone and related photochemical oxidants ([U.S. EPA, 2013](#)), particulate matter ([U.S. EPA, 2009](#)), and the second draft ISA for oxides of nitrogen ([U.S. EPA, 2015b](#))]. The Preamble is intended to serve multiple ISAs and as such will improve overall efficiency and consistency of the ISA process. The Preamble will be revised and updated as needed, and CASAC and public comments on the Preamble are welcome.

The Preface within the draft SO_x ISA outlines the legislative requirements and history of the reviews of the primary SO₂ NAAQS. Chapter 1 of the draft SO_x ISA provides an integrative summary and conclusions of this assessment. Chapter 1 is supported by subsequent chapters that provide detailed information on the relevant evidence available from the multiple disciplines that inform our understanding of the health effects of gaseous sulfur oxides: atmospheric chemistry and ambient concentrations of sulfur oxides (Chapter 2); exposure to ambient sulfur oxides (Chapter 3); dosimetry and modes of action (Chapter 4); health effects of short-term and long-term exposure to sulfur oxides (Chapter 5); and lifestages and populations potentially at increased risk for health effects related to sulfur oxides (Chapter 6). The final SO_x ISA, in conjunction with additional technical assessments, will provide the scientific basis for the U.S. EPA's decision regarding the adequacy of the primary NAAQS for SO₂ to protect human health.

This review of the primary SO₂ NAAQS was initiated in May 2013 with a call for information from the public (78 FR 27387). In June 2013, the U.S. EPA held a workshop titled "Workshop to Discuss Policy-Relevant Science to Inform the U.S. EPA's Integrated Plan for Review of the National Ambient Air Quality Standards for Sulfur Oxides" co-organized by NCEA and the U.S. EPA's Office of Air Quality Planning and Standards (OAQPS) (78 FR 27387). In March 2014, a draft Integrated Review Plan (IRP) for the Review of the Primary SO₂ Standard was made available for public comment (79 FR 14035) and was discussed by the CASAC Augmented for Sulfur Oxides Panel via a publicly accessible teleconference consultation in April 2014. (79 FR 16325). The final IRP was released in December 2014 (EPA-452/R-14-007). In June 2014, NCEA held a public workshop to discuss, with invited scientific experts, initial draft materials prepared in the development of the draft SO_x ISA (79 FR 33750). Preparation of the External Review Draft SO_x ISA benefitted both from that CASAC consultation and from the peer input workshop.

The purpose of this memo is to provide the CASAC Augmented for Sulfur Oxides Panel with charge questions related to a number of important topics addressed in the draft SO_x ISA. Following the CASAC and public review of the draft SO_x ISA, NCEA-RTP will release a revised version of the SO_x ISA, anticipated for fall 2016.

Charge to the CASAC Augmented for Sulfur Oxides Panel

The U.S. EPA has aimed to succinctly present and integrate the policy-relevant scientific evidence for the review of the SO₂ NAAQS while also sufficiently describing how scientific information was evaluated in forming the conclusions presented. Previous panels have emphasized the importance of older studies and concluded that if older studies are open to reinterpretation in light of newer data and/or they remain the definitive works available in the literature, they should be discussed in detail to reinforce key concepts and conclusions. In considering subsequent charge questions and recognizing an overall goal of

producing a clear and concise document, are there topics that should be added or receive additional discussion? Similarly, are there topics for which discussion should be shortened or removed? Does the Panel have opinions on how the document can be shortened without eliminating important and necessary content?

In addition, we ask the Panel to focus on the following specific questions in their review:

1. The Executive Summary is intended to provide a concise synopsis of the key findings and conclusions of the SO_x ISA for a broad range of audiences. Please comment on the clarity with which the Executive Summary communicates the key information from the SO_x ISA. Please provide recommendations on information that should be added or information that should be left for discussion in the subsequent chapters of the SO_x ISA.
2. Chapter 1 summarizes key information from the Preamble about the process for developing an ISA. Chapter 1 also presents the integrative summary and conclusions from the subsequent detailed chapters of the SO_x ISA and characterizes available scientific information on policy-relevant issues.
 - a. Please comment on the usefulness and effectiveness of the summary presentation. Please provide recommendations on approaches that may improve the communication of key findings to varied audiences and the synthesis of available information across subject areas. What information should be added or is more appropriate to leave for discussion in the subsequent detailed chapters?
3. Chapter 2 describes scientific information on sources, atmospheric chemistry, and measurement and modeling of ambient concentrations of gaseous sulfur oxides.
 - a. To what extent is the information presented regarding sources, chemistry, and measurement and modeling of ambient concentrations accurate, complete, and relevant to the review of the SO₂ NAAQS?
 - b. Please comment on the extent to which available information on the spatial and temporal trends of ambient SO₂ concentrations at various scales has been adequately and accurately described. In particular, what is the extent to which the analyses of recently available 5-min SO₂ concentration data are informative in considering relationships between 5-min and 1-hr SO₂ concentrations?
 - c. How informative is the analysis of correlations between SO₂ and co-occurring pollutant concentrations for interpretation of epidemiologic studies?
4. Chapter 3 describes scientific information on exposure to ambient SO₂ and implications for epidemiologic studies.
 - a. To what extent is the discussion on methodological considerations for exposure measurement and modeling clearly and accurately conveyed, appropriately characterized, and relevant to the review of the SO₂ NAAQS?
 - b. Please comment on the accuracy, level of detail, and clarity of the discussion regarding exposure assessment and the influence of exposure error on effect estimates in epidemiologic studies of the health effects of SO₂.

5. Chapter 4 characterizes scientific evidence on the dosimetry and modes of action for SO₂. Dosimetry and modes of action are bridged by the absorption and reaction of SO₂ in the epithelial lining fluid to form SO₂-derived products (e.g., sulfite and/or S-sulfonates) that are widely distributed throughout the body.
 - a. To what extent is the discussion of the chemistry of inhaled SO₂ and the processes of absorption, distribution, metabolism, and elimination accurate, complete, and relevant to the review of the SO₂ NAAQS?
 - b. Please comment on the discussion comparing endogenously generated and ingested sulfite with that derived from ambient inhalation.
 - c. To what extent are the discussion and integration of the potential modes of action underlying the health effects of exposure to sulfur oxides presented accurately and in sufficient detail? Are there additional modes of action that should be included in order to fully characterize the underlying mechanisms of sulfur oxides?
6. Chapter 5 presents assessments of the health effects associated with short-term and long-term exposure to sulfur oxides. The discussion is organized by health effect category, exposure duration, outcome, and scientific discipline.
 - a. To what extent does this chapter accurately reflect the body of evidence from previous and recent epidemiologic, controlled human exposure and toxicological studies? What are the views of the panel on the integration of this evidence and the relative emphasis placed on each source of evidence?
 - b. Considering the discussion of the strengths and limitations of the evidence in the text and tables within Chapter 5, to what extent is the causal framework appropriately applied to evidence for each of the health effect categories to form causal determinations?
 - c. The conclusions in the draft SO_x ISA regarding the respiratory effects of SO₂ exposure rely heavily on controlled human exposure evidence demonstrating effects of short-term peak exposures. Interpretation of the epidemiologic studies is more complicated due to the longer averaging time used in these studies. Please comment on the extent to which the evidence pertaining to the lowest concentrations associated with effects is appropriately characterized.
7. Chapter 6 evaluates scientific information and presents conclusions on factors that may modify exposure to SO₂, physiological responses to SO₂ exposure, or risk of health effects associated with SO₂ exposure. Consistent with previous ISAs for ozone, lead, and oxides of nitrogen, conclusions on these at-risk factors inform at-risk lifestages and populations.
 - a. To what extent has the available scientific evidence from epidemiologic, controlled human exposure, and toxicological studies been integrated to inform conclusions on at-risk populations and/or lifestages? Is there information available on other key at-risk factors that is not included in the draft SO_x ISA and should be added?

We look forward to discussing these issues with the CASAC Augmented for Sulfur Oxides Panel at our upcoming meeting. Should you have any questions regarding the draft SO_x ISA, please feel free to contact Dr. Steven Dutton (919-541-5035, dutton.steven@epa.gov) or Dr. Tom Long (919-541-1880, long.tom@epa.gov).

cc: Steven Dutton, ORD/NCEA
Lynn Flowers, ORD/NCEA
Nicole Hagan, OAR/OAQPS
Bob Hetes, OAR/OAQPS
John Langstaff, OAR/OAQPS
Tom Long, ORD/NCEA
Kenneth Olden, ORD/NCEA
Mary Ross, ORD/NCEA
Erika Sasser, OAR/OAQPS
Debra Walsh, ORD/NCEA
Karen Wesson, OAR/OAQPS