EPA United States Environmental Protection Agency

Integrated Plan for Review of the Primary National Ambient Air Quality Standards for Sulfur Oxides

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DISCLAIMER

This integrated review plan serves as a public information document and as a management tool for the U.S. Environmental Protection Agency's National Center for Environmental Assessment and the Office of Air Quality Planning and Standards in conducting the review of the national ambient air quality standards for sulfur oxides. The approach described in this plan may be modified to reflect information developed during this review and to address advice and comments received from the Clean Air Scientific Advisory Committee and the public throughout this review. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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1. INTRODUCTION

The U.S. Environmental Protection Agency (EPA) is conducting a review of the primary (health-based) and secondary (welfare-based) national ambient air quality standards (NAAQS) for sulfur oxides (SO_x). The purpose of this document is to communicate the plan for this review. The review of the secondary NAAQS for SO_x, to be conducted in conjunction with the review of the secondary NAAQS for nitrogen oxides (NO_x), is being addressed in a separate plan.

This review will provide an integrative assessment of relevant scientific information for gaseous SO_x and will focus on the basic elements of the primary standards: the indicator, averaging times, forms,[1] and levels. These elements, which serve to define each ambient air quality standard, must be considered collectively in evaluating the health protection afforded by the standard. The current primary standards use SO_2 as the indicator for the broader mix of gaseous SO_x in the ambient air. The existing primary SO_2 standards include a 24-hour standard set at 0.14 parts per million (ppm), not to be exceeded more than once per year, and an annual standard set at 0.03 ppm, calculated as the arithmetic mean of hourly averages.

This review plan is organized into six chapters. Chapter 1 presents background information on the review process, the legislative requirements for the review of the NAAQS, past reviews of the SO_2 NAAQS, and the scope of the current review. Chapter 2 presents the current review schedule. Chapter 3 presents a set of policy-relevant questions that will serve to focus this review on the critical scientific and policy issues. Chapters 4 through 6 discuss the planned scope and organization of the key assessment documents, the planned approaches for preparing the documents, and plans for scientific and public review of the documents.

1.1 OVERVIEW OF THE REVIEW PROCESS

The Agency has recently decided to make a number of changes to the process for reviewing the NAAQS (described at http://www.epa.gov/ttn/naaqs/). In making these changes, the Agency consulted with the Clean Air Scientific Advisory Committee (CASAC), which provides advice to the Administrator on key elements of NAAQS reviews, and the public. This

[1] The "form" of a standard defines the air quality statistic that is to be compared to the level of the standard in determining whether an area attains the standard.

new process, which is being applied to the current review of the SO_2 NAAQS, contains four major components. Each of these components is described in this section.

The first component of the review process is the development of an integrated review plan. This plan presents the schedule for the review, the process for conducting the review, and the key policy-relevant science issues that will guide the review. The final integrated review plan will be informed by input from CASAC, outside scientists, and the public. For purposes of this review (and for the Agency's concurrent review of the NO_2 primary NAAQS), the 7-member CASAC has been supplemented by additional scientific experts, collectively referred to as the CASAC NO_x and SO_x Primary Review Panel (see appendix).

The second component of the review process is a science assessment. Under the new process, a concise synthesis of the most policy-relevant science will be compiled into an Integrated Science Assessment (ISA), which will be informed by input from CASAC, outside scientists, and the public. The ISA for this review of the SO_2 NAAQS will critically evaluate and integrate scientific information on the health effects associated with exposure to SO_x in the ambient air. It will focus on scientific information that has become available since the last review and will reflect the current state of knowledge on the most relevant issues pertinent to the review of the primary SO_2 NAAQS. The ISA will be supported by more detailed information about the scientific literature, which will be compiled into a series of annexes. Together, the ISA and its annexes will replace the Air Quality Criteria Document from previous NAAQS reviews.

The third component of the review process is a risk/exposure assessment, which will be informed by input from CASAC, outside scientists, and the public. This assessment will develop, as appropriate, quantitative estimates of human exposures and risk associated with current ambient levels of SO_2, with levels that just meet the current standard, and with levels that just meet possible alternative standards. EPA will then prepare a concise report that focuses on key results, observations, and uncertainties.

The fourth component of the revised process is a policy assessment/rulemaking. Under the new process, a staff paper, such as that prepared in previous NAAQS reviews, will not be prepared. Rather, Agency views on policy options will be published in the Federal Register as an advance notice of proposed rulemaking (ANPR). The ANPR will present a policy assessment and will be accompanied by supporting documents, such as air quality analyses and technical support documents, as appropriate. Taking into account CASAC advice and recommendations

as well as public comment on the ANPR, the Agency will publish a proposed rule, to be followed by a public comment period. Considering comments received on the proposed rule, the Agency will issue a final rule to complete the rulemaking process.

1.2 LEGISLATIVE REQUIREMENTS

Two sections of the Clean Air Act (CAA) govern the establishment and revision of the NAAQS. Section 108 (42 U.S.C. 7408) directs the Administrator to identify and list "air pollutants" that "in his judgment, may reasonably be anticipated to endanger public health and welfare" and whose "presence . . . in the ambient air results from numerous or diverse mobile or stationary sources" and to issue air quality criteria for those that are listed. Air quality criteria are intended to "accurately reflect the latest scientific knowledge useful in indicating the kind and extent of identifiable effects on public health or welfare which may be expected from the presence of [a] pollutant in ambient air . . . ."

Section 109 (42 U.S.C. 7409) directs the Administrator to propose and promulgate "primary" and "secondary" NAAQS for pollutants listed under section 108. Section 109(b)(1) defines a primary standard as one "the attainment and maintenance of which in the judgment of the Administrator, based on such criteria and allowing an adequate margin of safety, are requisite to protect the public health."[2] A secondary standard, as defined in section 109(b)(2), must "specify a level of air quality the attainment and maintenance of which, in the judgment of the Administrator, based on such criteria, is required to protect the public welfare from any known or anticipated adverse effects associated with the presence of [the] pollutant in the ambient air."[3]

The requirement that primary standards include an adequate margin of safety was intended to address uncertainties associated with inconclusive scientific and technical information available at the time of standard setting. It was also intended to provide a reasonable

[2] The legislative history of section 109 indicates that a primary standard is to be set at "the maximum permissible ambient air level . . . which will protect the health of any [sensitive] group of the population," and that for this purpose "reference should be made to a representative sample of persons comprising the sensitive group rather than to a single person in such a group" [S. Rep. No. 91-1196, 91st Cong., 2d Sess. 10 (1970)].

[3] Welfare effects as defined in section 302(h) [42 U.S.C. 7602(h)] include, but are not limited to, "effects on soils, water, crops, vegetation, man-made materials, animals, wildlife, weather, visibility and climate, damage to and deterioration of property, and hazards to transportation, as well as effects on economic values and on personal comfort and well-being."

degree of protection against hazards that research has not yet identified. See *Lead Industries Association v. EPA*, 647 F.2d 1130, 1154 (D.C. Cir 1980), cert. denied, 449 U.S. 1042 (1980); *American Petroleum Institute v. Costle*, 665 F.2d 1176, 1186 (D.C. Cir. 1981), cert. denied, 455 U.S. 1034 (1982). Both kinds of uncertainties are components of the risk associated with pollution at levels below those at which human health effects can be said to occur with reasonable scientific certainty. Thus, in selecting primary standards that include an adequate margin of safety, the Administrator is seeking not only to prevent pollution levels that have been demonstrated to be harmful but also to prevent lower pollutant levels that may pose an unacceptable risk of harm, even if the risk is not precisely identified as to nature or degree.

In selecting a margin of safety, the EPA considers such factors as the nature and severity of the health effects involved, the size of sensitive population(s) at risk, and the kind and degree of the uncertainties that must be addressed. The selection of any particular approach to providing an adequate margin of safety is a policy choice left specifically to the Administrator's judgment. See *Lead Industries Association v. EPA*, supra, 647 F.2d at 1161-62.

In setting standards that are "requisite" to protect public health and welfare, as provided in section 109(b), EPA's task is to establish standards that are neither more nor less stringent than necessary for these purposes. In so doing, EPA may not consider the costs of implementing the standards. See generally *Whitman v. American Trucking Associations*, 531 U.S. 457, 465-472, 475-76 (2001).

Section 109(d)(1) requires that "not later than December 31, 1980, and at 5-year intervals thereafter, the Administrator shall complete a thorough review of the criteria published under section 108 and the national ambient air quality standards . . . and shall make such revisions in such criteria and standards and promulgate such new standards as may be appropriate . . . ." Section 109(d)(2) requires that an independent scientific review committee "shall complete a review of the criteria . . . and the national primary and secondary ambient air quality standards . . . and shall recommend to the Administrator any new . . . standards and revisions of existing criteria and standards as may be appropriate . . . ." Since the early 1980's, this independent review function has been performed by the Clean Air Scientific Advisory Committee (CASAC) of EPA's Science Advisory Board.

1.3 HISTORY OF REVIEWS FOR THE PRIMARY SO_2 NAAQS

On April 30, 1971, the EPA promulgated primary SO_2 NAAQS. These primary standards, which were based on the findings outlined in the original 1969 Air Quality Criteria for Sulfur Oxides, were set at 0.14 parts per million (ppm) averaged over a 24-hour period, not to be exceeded more than once per year, and 0.030 ppm annual arithmetic mean. In 1982, EPA published the *Air Quality Criteria for Particulate Matter and Sulfur Oxides* (EPA, 1982) along with an addendum of newly published controlled human exposure studies, which updated the scientific criteria upon which the initial standards were based (EPA, 1982). In 1986, a second addendum was published presenting newly available evidence from epidemiologic and controlled human exposure studies (EPA, 1986). In 1988, EPA published a proposed decision not to revise the existing standards (53 FR 14926). However, EPA specifically requested public comment on the alternative of revising the current standards and adding a new 1-hour primary standard of 0.4 ppm.

As a result of public comments on the 1988 proposal and other post-proposal developments, EPA published a second proposal on November 15, 1994 (59 FR 58958). The 1994 re-proposal was based in part on a supplement to the second addendum of the criteria document, which evaluated new findings on short-term SO_2 exposures in asthmatics (EPA, 1994a). As in the 1988 proposal, EPA proposed to retain the existing 24-hour and annual standards. The EPA also solicited comment on three regulatory alternatives to further reduce the health risk posed by exposure to high 5-minute peaks of SO_2 if additional protection were judged to be necessary. The three alternatives were: 1) Revising the existing primary SO_2 NAAQS by adding a new 5-minute standard of 0.60 ppm SO_2; 2) establishing a new regulatory program under section 303 of the Act to supplement protection provided by the existing NAAQS, with a trigger level of 0.60 ppm SO_2, one expected exceedance; and 3) augmenting implementation of existing standards by focusing on those sources or source types likely to produce high 5-minute peak concentrations of SO_2. On May 22, 1996, EPA's final decision, that revisions of the NAAQS for SO_x were not appropriate at that time, was announced in the Federal Register (61 FR 25566). In that decision, EPA announced an intention to propose guidance, under section 303 of the Act, to assist states in responding to short-term peak levels of SO_2. The basis for the decision, and subsequent litigation, is discussed below in Chapter 3.

1.4 SCOPE OF THE REVIEW

As noted above, in reviewing the SO_2 NAAQS, EPA has historically focused its review of relevant scientific information on the broad category of sulfur oxides, while finding it appropriate to specify the indicator of the standard specifically in terms of SO_2. The sulfur oxides include multiple gaseous (e.g., SO_2, SO_3) and particulate (e.g., sulfate) species, both of which will be considered in characterizing the atmospheric chemistry of SO_x. Although we anticipate that the majority of the information available to inform the current review, particularly with regard to human exposures and health effects, will be specifically for SO_2, we will consider the other gaseous sulfur oxides to the extent that information is available and relevant to the review of the SO_2 NAAQS. In addition, we will consider the possible influence of atmospheric pollutants other than the sulfur oxides (e.g., nitrogen oxides, carbon monoxide, ozone, particulate matter) on the interpretation of the role of sulfur oxides in health effects studies.

In considering what species of SO_x are relevant to the review of the SO_2 NAAQS, we note that the health effects associated with particulate species of sulfur oxides have been considered within the context of the health effects of ambient particles in the Agency's review of the NAAQS for particulate matter (PM). Thus, the current review of the SO_2 NAAQS will focus on the gaseous species of sulfur oxides and will not consider health effects directly associated with particulate species of sulfur oxides. In the most recent review of the NAAQS for PM, it was determined that size-fractionated particle mass, rather than particle composition, remains the most appropriate approach for addressing ambient PM. This conclusion will be re-assessed in the next review; however, at present it would be redundant to also use the SO_2 NAAQS to protect against the health effects of particulate sulfur oxides.

2. REVIEW SCHEDULE

In May of 2006, EPA's National Center for Environmental Assessment in Research Triangle Park, NC (NCEA-RTP) announced the initiation of the current periodic review of the air quality criteria for SO_x and the SO_2 NAAQS and issued a call for information in the Federal Register (71 FR 28023). Table 2-1 outlines the anticipated schedule for this review.[4]

Table 2-1. Anticipated Schedule for Development of Revised SO_x Integrated Science Assessment (ISA) and SO_2 Primary Standard

Stage of Review	Major Milestone	Draft Target Dates
Integrated Plan	Literature Search	Ongoing
	Call for Information	May 2006
	Draft Integrated Review Plan	April 2007
	Workshop on science/policy issues	February 2007
	CASAC/public consultation on draft plan	May 2007
	Final Integrated Review Plan	October 2007
Science Assessment	First draft of ISA	September 2007
	CASAC/public review of first draft ISA	December 2007
	Second draft of ISA	April 2008
	CASAC/public review of second draft ISA	July 2008
	Final ISA	September 2008
Risk/Exposure Assessment	Assessment methodology	October 2007
	CASAC/public comment on methodology	December 2007
	First draft risk/exposure assessments	May 2008
	CASAC/public review of first draft assessments	July 2008
	Second draft of risk/exposure assessment	October 2008
	CASAC/public review of second draft assessments	December 2008
	Final assessments	January 2009
Policy Assessment/Rulemaking	ANPR	February 2009
	CASAC review/public comment on ANPR	April 2009
	Proposed rulemaking	July 2009
	Final rulemaking	March 2010

[4] This schedule is provisional, subject to completion of the settlement process and entry of an appropriate court order in *Center for Biological Diversity et al. v. Johnson* (D.D.C) Civ. No. 05-01814

3. KEY POLICY-RELEVANT ISSUES

3.1 HISTORICAL PERSPECTIVE

The first SO_2 NAAQS was established in 1971. At that time, a 24-hour standard of 0.14 ppm, not to be exceeded more than one time per year, and an annual standard of 0.03 ppm were judged to be both adequate and necessary to protect public health. The most recent review of the SO_2 NAAQS was completed in 1996 and focused on the question of whether an additional short-term standard (e.g., 5-minute) was necessary to protect against short-term, peak exposures. Based on the scientific evidence, the administrator judged that repeated exposures to 5-minute peak SO_2 levels ($\geq$0.60 ppm) could pose a risk of significant health effects for asthmatic individuals at elevated ventilation rates. The Administrator also concluded that the likely frequency of such effects should be a consideration in assessing the overall public health risks. Based upon an exposure analysis conducted by EPA, the Administrator concluded that exposure of asthmatics to SO_2 at levels that can reliably elicit adverse health effects is likely to be a rare event when viewed in the context of the entire population of asthmatics. Therefore, 5-minute peak SO_2 levels were judged not to pose a broad public health problem when viewed from a national perspective, and a 5-minute standard was not promulgated.

The American Lung Association and the Environmental Defense Fund challenged EPA's decision not to establish a 5-minute standard. On January 30, 1998, the Court of Appeals for the District of Columbia found that EPA had failed to adequately explain its determination that no revision to the SO_2 NAAQS was appropriate and remanded the decision back to EPA for further explanation. Specifically, the court required EPA to provide additional rationale to support the Agency judgment that 5-minute peaks of SO_2 do not pose a public health problem from a national perspective even though these peaks will likely cause adverse health impacts in a subset of asthmatics. In response, EPA has collected and analyzed additional air quality data focused on 5-minute concentrations of SO_2. These air quality analyses conducted since the last review will help inform the current review, which will address issues raised in the Court's remand of the Agency's last decision. No further Agency action has been taken.

3.2 ISSUES TO BE CONSIDERED IN THE CURRENT REVIEW

In this review, a series of policy-relevant questions will frame our approach to determining whether the current primary SO_2 NAAQS should be retained or revised. The answers to these questions, and the resulting conclusions regarding the corresponding policy issues, will inform the decision of whether to retain or revise the current standards, and/or whether to set an additional standard to protect against short term, peak exposures.

The first step in reviewing the adequacy of the current primary SO_2 standard is to consider whether the available body of scientific evidence supports or calls into question the scientific conclusions reached in the last review regarding health effects related to exposure to SO_2 and other gaseous oxides of sulfur (collectively referred to subsequently in this plan as SO_x) in the ambient air. This evaluation of the newly available scientific evidence will address a series of questions including the following.

- Has new information altered/substantiated the scientific support for the occurrence of health effects following short- and/or long-term exposure to levels of SO_x found in the ambient air?
- Does new information impact conclusions from the previous review regarding the effects of SO_x on susceptible populations?
- At what levels of SO_x exposure do health effects of concern occur?
- Has new information altered conclusions from previous reviews regarding the plausibility of adverse health effects caused by SO_x exposure?
- To what extent have important uncertainties identified in the last review been reduced and/or have new uncertainties emerged?
- What are the air quality relationships between short-term and longer-term exposures to SO_x?

If the evidence suggests that revision of the current standard might be appropriate, we will consider whether the available body of evidence supports consideration of alternative standards. The following questions will inform this determination.

- Is there evidence for the occurrence of adverse health effects at levels of SO_x lower than those observed previously? If so, at what levels and what are the important uncertainties associated with that evidence?

- Do exposure estimates suggest that levels of concern for SO_x-induced health effects will occur with current ambient levels of SO_2, or with levels that just meet the current, or potential alternative standards? If so, are these exposures of sufficient magnitude such that the health effects might reasonably be judged to be important from a public health perspective? What are the important uncertainties associated with these exposure estimates?
- Do the evidence, the air quality assessment, and risk/exposure assessment, provide support for considering different standard indicators or averaging times?
- What range of levels is supported by the evidence, the air quality assessment, and risk/exposure assessment? What are the uncertainties and limitations in the evidence and assessments?
- What is the range of forms supported by the evidence, the air quality assessment, and risk/exposure assessment? What are the uncertainties and limitations in the evidence and assessments?

4. SCIENCE ASSESSMENT

4.1 SCOPE AND ORGANIZATION

The science assessment will consist of the ISA and its supporting annexes. The ISA will critically evaluate and integrate the scientific information on exposure and health effects associated with SO_x in ambient air.[5] The annexes, which will summarize relevant studies, will provide a detailed basis for developing the ISA. The ISA and accompanying annexes will include scientific evidence in the discipline areas of epidemiology, animal and human toxicology, and dosimetry as well as human exposure and atmospheric science relevant to the review of the primary SO_2 NAAQS. The ISA will synthesize the current state of knowledge on the most relevant issues pertinent to the review of the SO_2 NAAQS. Discussions in the ISA will focus on the key policy questions described in Chapter 3 of this document. The ISA will synthesize information on the health effects of SO_x drawing from the disciplines noted above. These discussions will be placed in the context of the atmospheric environment (i.e, those aspects that consider the nature, sources, distribution, measurement, and/or concentrations of SO_x in ambient air). The ISA will also evaluate available information relevant to assessing human exposures and risks to public health associated with these exposures.

The focus of the ISA will be on literature published since the previous review of the air quality criteria for SO_x. Key findings and conclusions from the 1982 Air Quality Criteria Document and First Addendum (EPA, 1982), the 1986 Second Addendum (EPA, 1986), and the 1994 Supplement to the Second Addendum (EPA, 1994a) will be briefly summarized at the beginning of the ISA. The results of recent studies will be integrated with previous findings. Important older studies will be more specifically discussed if they are open to reinterpretation in light of newer data. Generally, only information that has undergone scientific peer review and that has been published (or accepted for publication) in the open literature will be considered. In human and animal toxicologic studies, emphasis will be placed on studies conducted at or near SO_x concentrations found in ambient air. However, in recognition of the fact that toxicologic

[5] Note that evidence related to environmental effects of SO_x will be considered separately in the science assessment conducted as part of the review of the secondary NAAQS for NO_2 and SO_2.

studies do not necessarily reflect effects in the most sensitive populations, studies at higher exposure levels will be included when they provide information relevant to previously unreported effects, evidence of the potential mechanism for an observed effect, or information on exposure-response relationships.

4.2 ASSESSMENT APPROACH

Document Preparation

The NCEA-RTP is responsible for preparing the ISA and its annexes for SO_x. Expert authors will include EPA staff with an extensive base of knowledge in their respective fields and extramural scientists contracted to the EPA.

Literature Search

The NCEA-RTP uses a systematic approach to identify relevant studies for consideration. A Federal Register Notice is published to announce the initiation of a review and to request information from the public. An initial publication base is established by searching MEDLINE and other databases using as key words the following terms: sulfur oxides, sulfur dioxide, SO_x, SO_2, and reduced sulfur gases. This search strategy is periodically reexamined and modified to enhance identification of pertinent published papers. Additional papers are identified for inclusion in the publication base in several ways. First, EPA staff reviews pre-publication tables of contents for journals in which relevant papers may be published. Second, expert chapter authors are charged with independently identifying relevant literature. Finally, additional publications that may be pertinent are identified by both the public and CASAC during the external review process. The studies identified will include recently published or accepted for publication by a date determined to be as inclusive as possible given the relevant target dates in the NAAQS review schedule. Some additional studies, published after that date, may also be included if they provide new information that impacts one or more key scientific issues. The combination of these approaches should produce a comprehensive collection of pertinent studies for review in the annexes and to form the basis of the ISA.

Criteria for Study Selection

In selecting epidemiologic studies for the present assessment, EPA will consider whether a given study contains information on (1) short- or long-term exposures at or near ambient levels of SO_x; (2) health effects of specific SO_x species or indicators related to SO_2 sources; (3) health endpoints that repeat or extend findings from earlier assessments as well as those not previously researched; (4) susceptible and vulnerable populations to SO_x exposure; (5) multiple pollutant analyses and other approaches to address issues related to potential interactions (e.g., are there synergistic effects of SO_x with other pollutants), confounding (e.g., is SO_x associated with health endpoints independent of copollutants), and effect modification (e.g., is the effect of SO_x on health endpoints modified by the presence of copollutants); and/or (6) important methodological issues (e.g., lag of effects, model specifications, thresholds, mortality displacement) related to SO_x effects. Among the epidemiologic studies, particular emphasis is focused on those relevant to standard setting in the United States. Specifically, studies conducted in the United States or Canada will be generally accorded more text discussion than those from other geographic regions, as the potential impacts of different health care systems and the underlying health status of populations need to be accounted for in the assessment. In addition, emphasis in the text is placed on discussion of (1) new, multi-city studies that employ standardized methodological analyses for evaluating SO_x effects, provide overall estimates for effects based on combined analyses of information pooled across cities, and examine results for consistency across cities; (2) new studies that provide quantitative effect estimates for populations of interest; and (3) studies that regard SO_x as a component of a complex mixture of air pollutants and thus give consideration to the levels of other copollutants, correlations of SO_x with these copollutants, and conduct multipollutant analyses.

A set of explicit criteria will also be used to select experimental studies for discussion. The selection of research evaluating controlled exposures of laboratory animals will focus primarily on those studies conducted at or near ambient SO_x concentrations and those studies that approximate expected human exposure conditions in terms of concentration and duration, which will depend on the toxicokinetics and biological sensitivity of the particular laboratory animal examined. In discussing the mechanisms of SO_x toxicity, studies conducted under atmospherically relevant conditions will be emphasized whenever possible, but studies at higher levels also will be considered, due to species-to-species differences and potential differences in

sensitivity between study subjects and especially susceptible human populations. For research evaluating controlled human exposures to SO_x, emphasis will be placed on studies that (1) investigate effects on potentially susceptible populations such as asthmatics, particularly studies where subjects serve as their own control to compare responses following SO_x exposure and sham exposure and where responses in susceptible individuals are compared with those in age-matched healthy controls; (2) address issues such as dose-response or time-course of responses; (3) investigate exposure to SO_x separately and in combination with other pollutants; (4) include controlled exposures to filtered air; and (5) have sufficient sample size to adequately assess findings.

Content and Organization of the ISA

The organization of the ISA for SO_x will be consistent with that used in the integrative chapter of the criteria document for O_3 (U.S. Environmental Protection Agency, 2006). The ISA will contain information relevant to considering whether it is appropriate to retain or revise the current short-term and annual standard and whether it is appropriate to consider setting a separate short-term peak exposure standard. The content of the ISA will be guided by a series of policy-relevant questions that were derived from the previous review of the SO_2 NAAQS, as well as policy-relevant questions based on new scientific information. These policy-relevant questions are related to two overarching issues. The first issue is whether new evidence reinforces or calls into question the evidence presented and evaluated in the last NAAQS review. The second issue is the extent to which uncertainties from the last review have been addressed and/or whether new uncertainties have emerged. Specific questions that stem from these issues are listed below by topic area.

Air Quality and Atmospheric Chemistry: The ISA will present and evaluate data related to ambient concentrations of SO_x; sources leading to the presence of SO_x in the atmosphere; and chemical reactions that determine the formation, degradation, and lifetime of SO_x in the atmosphere.

- What are the strengths and weaknesses of various methods for measuring SO_x?
- Based on recent air quality and emissions data, what are current concentrations and emissions of SO_x? What spatial and temporal patterns can be seen in the air quality data for SO_x?

- Using air quality and emissions data as well as atmospheric chemistry models, what are the likely policy relevant background concentrations of SO_x?

Exposure: The ISA will evaluate the factors that influence exposure to SO_x and the uncertainties associated with extrapolation from ambient concentrations to personal exposures to SO_x of ambient origin, particularly in the context of interpreting results from epidemiologic studies. The issues of uncertainty differ by the exposure period of interest as short-term exposure studies (e.g., population-level studies using time-series analyses, field/panel studies) rely on temporal variation in exposure while long-term exposure studies (e.,g., longitudinal cohort studies) rely on spatial variability of exposure.

- What are the uncertainties when extrapolating between stationary SO_x monitoring instruments and personal exposure to SO_x of ambient origin, especially for susceptible groups? Issues include measurement error in outdoor ambient monitors, the use of centralized monitors for estimating community concentrations, and their use as a surrogate for personal exposure to SO_x of ambient origin.
- What do SO_2 concentrations from centrally-located ambient monitors represent? To what extent do they provide an estimate of ambient exposures to SO_2 versus an indicator of exposure to long range transport of pollutants from coal- or oil-fired power plants?
- What data are available to interpret SO_x exposures? This includes such information as air exchange rates and methods for measuring personal exposures to SO_x.
- How do SO_x exposures interact with other pollutant exposures, including PM and other gaseous copollutants?

Health Effects: The ISA will evaluate the literature related to respiratory, cardiovascular, and other health effects of SO_x exposure. Health effects that occur following both short- and long-term exposures will be evaluated in epidemiologic, human clinical, and toxicologic studies. Efforts will be directed at identifying the lowest levels at which effects are observed.

Short-Term Exposure:

- What do controlled human exposure, animal toxicologic, and epidemiologic studies indicate regarding the relationship between short-term (e.g., 24-hour average) and peak (e.g., 5-minute average) repeated exposures to SO_x and health effects of concern (e.g., respiratory symptoms, lung function decrements, inflammation, cardiovascular health endpoints, emergency department visits, hospital admissions, mortality) , including nature and time course, in healthy individuals and in those with preexisting disease states (e.g., asthmatics, cardiovascular disease) or preexisting susceptibility (e.g., genetic, biochemical)?
- How do results of recent studies expand current understanding of the relationship between repeated, short-term exposure to SO_x and lung function changes or lung function development? What are the lowest levels of SO_x at which these lung function effects are observed? What is the potential clinical relevance of these lung function effects?
- What are the effects of SO_x exposure on small airway function in humans (e.g., oxygen diffusion capacity, ventilation-perfusion mismatches) and what is the potential clinical relevance of these effects?
- What are the effects of SO_x exposure on cardiovascular health in humans (e.g., heart rate variability, arrhythmias, endothelial function, risk of myocardial infarction) and what is the potential clinical relevance of these effects?
- Is exposure to SO_x associated with mortality (total, respiratory, and/or cardiovascular), hospital admissions, and/or emergency department visits as assessed using population-level datasets? What are the lowest ambient SO_x concentrations at which these associations are observed? What are the uncertainties associated with this data?
- To what extent does exposure to SO_x contribute to health effects beyond the respiratory and cardiovascular systems?
- What is the nature of health effects following short-term exposure to multipollutant mixtures that contain SO_x in comparison to exposure to SO_x alone? Is there an interaction between SO_x and other air pollutants in the atmosphere?

- What influence do the patterns of SO_x exposure (i.e., peak, repeated peak, and average SO_x) have on evaluation of health effects?
- Do new data provide evidence to examine different exposure indices or averaging times specifically addressing the short-term standard and the need for a peak exposure standard?

Long-Term Exposure:

- Does the scientific evidence support the occurrence of health effects from long-term exposure (e.g., months to years) at ambient levels that are lower than previously observed? If so, what uncertainties are related to these associations and are the health effects in question important from a public health perspective?
- Can long-term exposures to SO_x result in chronic effects manifested as permanent lung tissue damage, reduction in baseline lung function, or impaired lung function development?
- To what extent does long-term SO_x exposure promote exacerbation and development of asthma or other chronic lung diseases, cardiovascular diseases, and other conditions? What is the relationship between long-term SO_x exposure and shortening of human life span via promotion of such diseases?
- To what extent does long-term exposure to SO_x contribute to other health effects, e.g., epigenetic and reproductive effects?
- How does long-term, low-level exposure to SO_x affect an individual's sensitivity to short-term but higher concentration exposures?
- What annual and seasonal patterns of SO_x exposure are most instrumental in promoting potentially harmful health effects?
- What is the nature of health effects following long-term exposure to multipollutant mixtures that contain SO_x in comparison to exposure to SO_x alone? Is there an interaction between SO_x and other air pollutants?
- Do new data provide evidence to examine different exposure indices or averaging times specifically addressing the long-term standard?

Causality: The ISA will evaluate the evidence as a basis for making inferences about the causal nature of associations between SO_x exposure and observed health outcomes. Key considerations in drawing conclusions about causality will be biological plausibility and coherence of the evidence. The ISA will place emphasis on studies conducted at typical ambient levels, except regarding evidence of biological plausibility and mechanisms, as these may only be observable in animal or human exposure study populations at higher levels than they might be observed in susceptible human populations.

- Does the evidence base contain new information to evaluate the case for or against a causal relationship between health effects and SO_x exposure?
- What information is available regarding the health impacts of a decrease in ambient levels of SO_x?

Uncertainties: The ISA will evaluate uncertainty in the scientific data, particularly in relation to observed epidemiologic findings.

- How does confounding by coexposure to other pollutants and by meteorological factors influence the uncertainty of the evidence base for both short- and long-term exposures?
- To what extent are the observed health effects associations attributable to SO_x versus the pollutant mixtures that SO_x may be representing? For example, ambient SO_2 concentrations may be serving as a surrogate measure for long range transport of particles.
- What are the uncertainties due to other confounding factors in epidemiologic studies (e.g., demographic and lifestyle attributes, genetic susceptibility factors, occupational exposure, and medical care)?
- What is the shape of the concentration-response curve (e.g., linear vs. threshold models) and how does this influence the public health impact?
- What uncertainties surround the evidence for long-term effects such as life shortening and development/progression of disease?

Biological Mechanisms of Action: The ISA will evaluate the data investigating biological mechanisms of action for the health outcomes associated with exposure to

SO_x. One limitation in examining mechanisms using animal toxicologic studies is the inherent anatomic and physiologic differences compared to humans that result in possible differences in dosimetry and mechanisms of action, especially with high exposure studies.

- Is there new information related to the biological mechanism of action?
- What are the potential biological mechanisms underlying response to SO_x, with a focus on physical-chemical characteristics, response pathway(s), and exposure-dose-response relationships?
- What are the inherent interspecies and interstrain differences in sensitivity to SO_x and in SO_x dosimetry in different regions of the respiratory tract and what are the implications of these differences?
- What are the interspecies and interstrain differences in basic mechanisms of lung injury and repair?
- What SO_x reaction products can be found in the respiratory tract cells, tissues, or fluids that may serve as markers of SO_x exposure?
- What are the effects of host factors such as age, gender, pre-existing disease, and genetic background on cellular and tissue responses to SO_x-induced injury?
- Which SO_x-induced health effects are sufficiently characterized to be quantitatively compared across species?
- What is the state of knowledge of laboratory animal-to-human extrapolation of effects? Is a credible qualitative extrapolation possible for short- and for long-term exposures?
- Do interactions with PM and other copollutants in the atmosphere influence the toxic potential of SO_x?

Susceptible and Vulnerable Populations: The ISA will examine health outcome data to identify specific groups that are more susceptible (e.g., children, asthmatics, patients with COPD, genetic susceptibility) and/or vulnerable (e.g., outdoor workers, socioeconomic factors) to the adverse effects of SO_x than normal healthy adults.

- What host and environmental factors (e.g., demographic, socioeconomic, and genetic) are associated with susceptibility and/or vulnerability to short- and long-term exposure to SO_x?
- Is preexisting respiratory or cardiovascular disease an important factor in susceptibility to mortality associated with exposure to SO_x and does age also play a role in this relationship?
- Regarding morbidity health endpoints, to what extent are specific subgroups more susceptible and/or vulnerable than the general population to SO_x exposure?
- What is the relationship, if any, between susceptibility to short- and long-term exposure to SO_x?
- Do interactions with PM and other copollutants in the atmosphere affect the susceptibility and/or vulnerability of humans to SO_x?

Public Health Impact: The ISA will present concepts related to the potential for defining adverse health effects. To accomplish this, the implications for public health of different health effects will be discussed. This will include, as appropriate, an estimation of the potential number of persons in sensitive sub-populations that are at increased risk for each health effect.

The ISA will be supplemented by a series of annexes, which will be focused on accomplishing two goals. The first goal will be to identify scientific research that is relevant to informing key policy issues. The second goal will be to produce a base of evidence containing all of the publications relevant to the SO_2 NAAQS review. The annexes will provide information on (1) the atmospheric chemistry of SO_x as well as the sampling/analytic methods for measurement of SO_x[6]; (2) human exposure to SO_x; (3) toxicologic studies of SO_x health effects; and (4) epidemiologic studies of health effects from short- and long-term exposure to SO_x. More detailed information on various methods and results for the health studies will be summarized in tabular form in the annex. These tables will generally be organized to include

[6] This section will also provide information on NO_2 in order to support the reviews of the primary and secondary NAAQS for both SO_2 and NO_2. The atmospheric chemistry of NO_x and SO_x are intricately linked. Therefore, discussion of their combined chemistry is more effective and more efficient than a separate discussion of each pollutant.

information about (1) concentrations of SO_x and averaging times; (2) description of study methods employed; (3) results and comments; and (4) quantitative outcomes for SO_x effect estimates.

In assessing the scientific quality and relevance of epidemiologic, animal toxicologic, and human controlled exposure studies, the following considerations will be taken into account: (1) to what extent are the aerometric data and exposure metrics of adequate quality and sufficiently representative to serve as credible exposure indicators; (2) were the study populations adequately selected and are they sufficiently well-defined to allow for meaningful comparisons between study groups; (3) are the health endpoint measurements meaningful and reliable; (4) are the statistical analyses appropriate, properly performed, and properly interpreted; (5) are likely covariates (i.e., potential confounders or effect modifiers) adequately controlled or taken into account in the study design and statistical analyses; and (6) are the reported findings internally consistent. Consideration of these issues will inform our judgments on the relative quality of individual studies and will allow us to focus the assessment on the most pertinent studies.

4.3 SCIENTIFIC AND PUBLIC REVIEW

Drafts of the ISA will be reviewed by CASAC. The annexes to the ISA will also be made available to CASAC in order to assist with their review; however, CASAC members (see Appendix) will not be specifically charged with reviewing the annexes. The CASAC NO_x/SO_x primary panel will review the draft document and discuss their comments in a public meeting announced in the Federal Register. Based on CASAC's past practice, EPA expects that key CASAC advice and recommendations for revision of the document will be summarized by the CASAC Chair in a letter to the EPA Administrator. In revising the draft ISA for SO_x, EPA will take into account any such advice and recommendations. EPA will also consider comments received, from CASAC or from the public, at the meeting itself and any written comments received. EPA anticipates preparing a second draft of the ISA for CASAC review and public comment. After appropriate revision, the final document will be made available on an EPA website and subsequently printed, with its public availability being announced in the Federal Register.

5. RISK/EXPOSURE ASSESSMENT

5.1 OVERVIEW

The risk/exposure assessments for the current review of the primary SO_2 NAAQS will be designed to estimate human exposures and to characterize the potential health risks that are associated with current ambient levels, with ambient levels that just meet the existing standard, and with ambient levels that just meet alternative standards that may be under consideration. The risk/exposure assessments will draw upon the information presented in the ISA and its Annexes. This includes information on atmospheric chemistry, air quality, human exposure, the impact of local source emissions, and health effects of concern. In particular, the availability of concentration-response and/or exposure-response data from the health effects literature will impact the type of risk and exposure assessments that would be performed.

Exposures will be assessed using a tiered approach where progression to a more sophisticated level of analysis will depend on the availability of data and on the anticipated utility of the results. For example, exposure may be assessed through the use of ambient air quality as a surrogate for exposure or may involve incorporating human activity data or possibly the development of individual exposure profiles. The particular form of the exposure assessment selected would generate ambient concentrations as well as exposure concentrations that are consistent with the available information on health effects associated with SO_2 exposure.

Risks would also be characterized using a tiered approach where progression to a more sophisticated level of analysis would depend on the availability of data and on the anticipated utility of the results. For example, risks could be assessed through the identification of concentration levels anticipated to result in adverse health effects, commonly termed potential health effect benchmarks. These potential health effect benchmarks could then used to determine how often air quality concentrations or estimated exposures exceed concentrations associated with adverse health effects. Concentration-response functions, derived from epidemiological studies, and/or exposure-response functions, derived from human clinical studies, may also be combined with air quality data or estimated exposures to characterize SO_2 health risk as appropriate and to the extent such information is available.

The major components of the risk/exposure assessments are outlined below and will be described in greater detail in a Scope and Methods Plan. Preparation of this detailed plan is underway and coincides with the development of the first draft ISA to facilitate the integration of policy-relevant science into both documents. This draft Scope and Methods Plan will also be the subject of a consultation with the CASAC NO_x/SO_x primary standard review panel and will be made available to the public for review and comment. The draft risk/exposure assessments prepared based on the Scope and Methods Plan will be made final upon completion of the final ISA and following review by the CASAC NO_x/SO_x primary standard review panel and the public.

5.2 OVERVIEW OF RISK/EXPOSURE ASSESSMENT FROM PRIOR REVIEW

In the previous review of the primary SO_2 NAAQS, exposure was assessed using two approaches (US EPA, 1982a; 1982b; 1986; 1994a; 1994b). Ambient monitor data served as a direct surrogate for exposure and emission estimates from targeted utility and non-utility sources of SO_2 were combined with exposure modeling and used to characterize potential local exposures. In addition to review of the existing standards of 0.14 ppm daily average and 0.030 ppm annual average, it was judged that repeated exposures to 5-minute peak SO_2 levels $\geq$0.60 ppm (noted here as 0.60 ppm-5min) could pose a risk of significant health effects for asthmatic individuals at elevated ventilation rates (e.g., while exercising). Therefore, the exposure analysis focused on exercising asthmatics and the potential for exposure to such short-term peak concentrations of SO_2.

First, an analysis of the existing ambient monitoring data was performed, where several exposure metrics were evaluated including the frequency of occurrence of 5-minute concentrations above 0.50, 0.60, and 0.70 ppm was determined, the number of repeated exceedances, and the sequential occurrences of peak concentrations within given a day (SAI, 1996). Several locations in the U.S. were reported to have a substantial number of short-term peak concentrations $\geq$0.60 ppm-5min in the vicinity of local sources. Then, a nationwide exposure assessment was conducted considering the frequency of exposure events $\geq$0.50 ppm-5min resulting from operation of utility boilers (Burton et al., 1987; Rosenbaum et al., 1992) and those originating from nonutility sources (Stoeckenius et al., 1990). The resultant exposure estimates indicated that between 0.7 and 1.8 percent of the total asthmatic population potentially

could be exposed one or more times per year, while outdoors at exercise, to SO_2 concentrations $\geq$0.50 ppm-5min. It was also noted that the frequency of exposures above a potential health effect benchmark of 0.60 ppm-5min, while not part of the analysis, would be anticipated to be lower. In addition, in response to the request for public comment on the 1994 reproposal, a revised exposure analysis was submitted for four of the larger nonutility sources by incorporating new data and using less conservative assumptions (Sciences International, Inc. 1995). Significantly fewer exposure events were estimated in this industry-sponsored revised analysis, decreasing the range of estimated exposures for these four sources by an order of magnitude (i.e., from 73,000-259,000 to 7,900-23,100).

Based upon the results of these analyses, it was concluded that exposure of asthmatics to SO_2 at concentrations that can elicit adverse health effects is likely to be a rare event when viewed in the context of the entire population of asthmatics (61 FR 25566). Therefore, 5-minute peak SO_2 concentrations were judged not to pose a broad public health threat when viewed from a national perspective, and the current standards of 0.14 ppm-24hr and 0.03 ppm-annual average were retained.

5.3 EXPOSURE ASSESSMENT APPROACH

A two-tiered approach to assessing exposure will be employed, beginning with an air quality analysis and progressing to a refined exposure analysis, if appropriate. This approach will be informed by the approach and results from the previous review of the SO_2 NAAQS (US EPA, 1982a; 1982b; 1986; 1994a; 1994b), subsequent analyses of air quality data focused on 5-minute concentrations of SO_2 (SAI, 1996), and the current SO_x ISA and relevant Annexes.

The goals of the SO_2 exposure assessment are: (1) to estimate short- and long-term exposures to ambient concentrations through air quality and modeling analyses that consider current air quality for SO_2 and air quality levels just meeting the current and any potential alternative SO_2 standards; (2) to develop quantitative relationships between short-term peak concentrations and time-averaged concentrations; and (3) to identify key assumptions and uncertainties in the exposure estimates. The exposure assessment will be used to inform the characterization of population risks, as described in Section 5.4.

Air Quality Characterization

The first step in assessing exposure will be to conduct an air quality analysis relying largely on ambient air quality data and the information provided in the ISA and relevant Annexes. In this analysis, the ambient SO_2 concentrations will serve as a surrogate for human exposure and will allow for comparison with the air quality evaluation performed in the previous review. This analysis will include information on SO_2 properties, current SO_2 air quality patterns, historic trends, policy-relevant background levels[7], and potential health effect benchmarks. The goal of the analysis is to build upon evaluations performed for the previous review (US EPA, 1994a) and to provide a frame of reference for subsequent discussions of the current standard and any possible alternative standards under consideration. General steps in the process include the following:

- Obtain available ambient monitoring data collected since the prior NAAQS review (e.g., 1996-2006), in particular hourly and any 5-minute time-averaged data (including continuous monitoring or reported maximum short-term peak concentrations)
- Estimate number of exceedances of short- and long-term averaging metrics, such as that of the current SO_2 standards (i.e., 0.03 ppm-annual and 0.14 ppm-daily) using recent monitoring data from individual sites (e.g., years 2003-2006)
- Estimate number of short-term peak concentrations (i.e., 5-minute averaging time) given just meeting the current SO_2 standards (both the daily and annual standards) and any potential alternative standards (using all available data)
    - Identify individual locations to evaluate that may contain higher than average number of short-term peak concentrations (if any). Criteria will be developed for selection of appropriate areas for analysis, possibly based on statistical comparisons of ambient concentrations and potential influence on ambient concentrations by local sources of SO_2 (e.g., presence of coal-fired power utilities). Note that in the prior review, analyses of 5-minute peaks indicated locations in Kentucky, Missouri, Montana, and West Virginia containing the greatest number of short-term peak concentrations above a potential health effect benchmark level of 0.60 ppm-5min (SAI, 1996).

[7] Policy-relevant background is defined as the distribution of SO_2 concentrations that would be observed in the U.S. in the absence of anthropogenic (man-made) emissions of SO_2 in the U.S., Canada, and Mexico.

- Evaluate the relationship between short-term (e.g., 5-minute) peak concentrations and concentrations over a one-hour averaging time. This would consider factors thought to influence peak-to-mean concentration ratios[8], possibly disaggregated by time-of-day, day-of-week, month-of-year, geographically, or given local source proximities, where relevant data exist.
- Develop predictive relationships to approximate the probability of occurrence of peak concentrations (e.g., 0.60 ppm-5min) given various averaging times (e.g., hourly, daily, annual) for use in locations without 5-minute ambient monitors.

- Estimate the number of short-term peak concentrations, categorized by population density proximal to ambient SO_2 monitors for where 5-minute monitoring was performed and for those where hourly monitoring was done.

The outcome of this air quality characterization is estimates of the number of short-term peak concentrations for use in estimating the number of exceedances of potential health effect benchmarks. In addition, air quality concentrations could be used in a health effects model that employs concentration-response functions, where relevant data are available and given appropriate averaging times (see Section 5.4).

Exposure Assessment

An exposure assessment would be designed to better represent the relationship between ambient concentrations, local sources, and human exposure. The approach would involve capturing variability in human exposure by representing important personal human attributes, such as time-location-activity patterns and human physiology, rather than assuming that ambient concentrations are equivalent to exposures. The assessment would consider several factors including:

- Factors that may contribute to greater personal exposures including the impacts of important sources of SO_2 (e.g., outdoor point sources such as coal-fired power utilities).
- Factors that may contribute to lessened personal exposures including the decay of SO_2 indoors.

[8] Previous analyses of 5-minute peak to 1-hour mean concentrations indicate on average the ratio of the two metrics is about 2, with larger ratios typically associated with the lowest 1-hour mean concentrations (SAI, 1996). Since there is likely greater variability in the peak-to-mean ratio at lower mean concentrations, distributions of ratios could be assigned for time-averaged concentration bins.

- Impact of human behavior (e.g., time spent indoors or outdoors, time spent near sources, timing of exposure event, breathing rate) in influencing the magnitude and duration of exposures, and frequency of repeated short-term peak exposures.
- Population living in close proximity to local sources.
- Exposures experienced by susceptible populations (e.g., asthmatic children).

In the prior review (US EPA, 1994a), a focused exposure analysis was performed considering short-term peak concentrations and the occurrence of potential short-term peak exposures in close proximity to local sources, since results of human clinical studies indicated a relationship between 5-minute peak SO_2 exposures and respiratory morbidity. The estimation of short-term SO_2 exposures remains as a key issue in this current NAAQS review and its associated exposure assessment due to the health effect conclusions drawn from the historical clinical data, the existence of a few new supporting clinical studies, and the occurrence of short-term peak concentrations near sources of SO_2 emissions. Critical to the approach is the development of fine spatial (e.g., within census tract) and temporal (e.g., 5-minute) air quality concentrations to better estimate exposures in areas where local point sources of SO_2 are identified. Short-term average ambient monitoring data are limited in abundance, both geographically and across site years, therefore local-scale dispersion modeling would be used to estimate spatially and temporally resolved concentrations proximal to identified emission sources.

The assessment approach would incorporate two main types of models: a model for estimating short-term peak concentrations within a distance of local emission sources of SO_2 and a model that simulates human contact with the estimated SO_2 air concentrations. The approach for estimating short-term peak concentrations would use AERMOD, a steady-state, Gaussian plume model (US EPA, 2004). AERMOD would estimate the time-series of SO_2 concentrations at selected receptor locations, which then can be supplied as input to an inhalation exposure model. Newly developed model input would be in the form of peak-to-hourly mean concentration ratio distributions, required for AERMOD to estimate 5-minute concentrations.

The latest version of EPA's Air Pollutants Exposure (APEX) model[9] (US EPA, 2006a; 2006b) would then be used to estimate exposures in this analysis. APEX is a Monte Carlo

simulation model that can be used to simulate a large number of randomly sampled individuals within specified locations, generating estimates of population exposure. APEX simulates exposures in indoor, outdoor, and in-vehicle microenvironments while taking into consideration the movement of individuals through time and space. Human activity data needed for this analysis would be drawn from the Consolidated Human Activity Database (CHAD) (McCurdy et al., 2000). Currently, the activity data already allow for exposure durations as short as one minute, however limited modification would be required for APEX to use the 5-minute ambient concentration data.

Results of this analysis would include the time series of exposure estimates for individuals within census tracts/blocks, proximal to identified local sources. These exposure estimates could be used either to estimate the number of exceedances of potential short- and long-term health effect benchmarks, or used in a health effects model that employs exposure-response functions, where appropriate data are available (see Section 5.4). Estimates would be developed for multiple indicators of exposure including 1) counts of people exposed one or more times to a given SO_2 concentration while at a specified breathing rate and 2) counts of person-occurrences of particular exposures, which may accumulate across persons in the population of interest.

5.4 RISK ASSESSMENT APPROACH

A two-tiered approach to characterizing health risks will be employed. In a first tier analysis, potential health effect benchmarks that may be identified based on information in the ISA would be combined with surrogate or exposure estimates from the exposure assessment in order to characterize population health risks. In a second tier risk analysis, which would be conducted only if judged appropriate and if relevant data are available, an assessment using concentration-response or exposure/dose-response data would be conducted by combining this data with either ambient air concentration distributions or exposure concentration distributions, respectively.

The goals of a SO_2 risk assessment would be: (1) to estimate the number of people exposed to SO_2 concentrations above potential health effect benchmarks considering current air quality and air quality levels just meeting the current and potential alternative SO_2 standards; (2)

[9] APEX is also referred to as the Total Risk Integrated Methodology/Exposure (TRIM.Expo) model (see

to provide distributions of health risk estimates over a range of ambient SO_2 concentrations; and (3) to identify key assumptions and uncertainties in the risk estimates.

Health Effect Benchmarks

This type of risk characterization would use exposure estimates, along with potential health effect benchmarks that may be identified based on information in the ISA and relevant Annexes, to estimate (1) the number of individuals with exposures above levels expected to cause adverse health effects, and (2) the range of the benchmark exceedance for those experiencing exposures of concern. Multiple exposure scenarios can be considered, including exposure associated with current ambient air quality, with current air quality levels enhanced by including local source contributions, and/or with levels of SO_2 associated with just meeting the current and potential alternative standards. Depending on data available in the ISA and Annexes, the health effect benchmarks may also account for those individuals that may be particularly susceptible and/or vulnerable to the effects of SO_2. The health risk characterization would require that averaging times be comparable for any estimated exposure concentrations and health metrics. For the purposes of this assessment, the approach is similar to calculating a hazard quotient which is the ratio of a weighted population exposure (or individuals in the case of the refined exposure assessment) to a potential health effect benchmark concentration.

Exposure-Response and Concentration-Response Functions

Incorporating exposure-response or concentration-response data in the risk characterization will depend on the availability of data from controlled human exposure studies and epidemiological studies, respectively. In either case, quantitative relationships provided by the study or derived from the data presented in the study describe the change in concentration (either ambient or exposure) associated with a change in health response. These relationships are then applied to estimate health risk.

Controlled human exposure studies involve volunteer subjects who are exposed to specified levels of SO_2 under controlled conditions for specified lengths of time. The responses reported previously include changes in respiratory function indicative of bronchoconstriction as measured by specific airway resistance (SR_{aw}) and decreased Forced Expiratory Volume in one

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http://www.epa.gov/ttn/fera/trim_gen.html for general details on TRIM).

second (FEV_1). These measures would form the basis for the development of exposure-response (E-R) relationships. Since the data are generated in a controlled laboratory setting, they can be applied in any area where exposures are either measured or modeled.

In contrast, epidemiological studies typically provide estimated concentration-response (C-R) relationships based on data collected in environmentally-relevant settings. Ambient SO_2 concentration would typically be measured as the average of monitor-specific measurements, although personal exposures may occasionally be measured. At the time of the prior review, there were no substantive epidemiological studies indicating relationships between SO_2 concentrations and adverse health effects. Again, depending on the type of health response function(s) available, ambient SO_2 concentration data would be used for characterizing risks, and would be most appropriately applied in areas where the epidemiological study was performed. It should be noted that a risk characterization based on epidemiological studies also requires baseline incidence rates and population data for the risk assessment locations.

Based on our current understanding of the available evidence, we do not anticipate that there will be sufficient E-R or C-R data from any new controlled clinical studies or epidemiological investigations to characterize health risk in this manner. Following review of the draft SO_x ISA and considering comments and recommendations by CASAC, the risk/exposure assessment scope and methods plan will be designed to include such a proposed approach to characterizing health risk if warranted.

5.5 ASSESSMENT CRITERIA

Criteria will be established to determine the level of detail warranted and the specific design of the assessments. The criteria will be designed to determine the value added to the assessment and for informing the SO_2 NAAQS decision. The factors identified below will be considered.

- Results of the ambient air quality characterization.
- Weight-of-evidence, as provided in the ISA, from new clinical studies with relevant exposure-response data, particularly those conducted at or near current ambient concentrations.
- Weight-of-evidence, as provided in the ISA, from new epidemiological studies that evaluate the relationship between short- and long-term exposures and health outcomes.

- New and relevant information regarding susceptible populations identified in previous reviews (e.g., asthmatics at an increased ventilation rate) or information regarding newly identified susceptible populations in the ISA.
- New and relevant information on the potential impact of point sources on residents within close proximity to such sources.
- Existence of the data required to perform the analyses in the more refined tiers of the assessment.

5.6 UNCERTAINTY AND VARIABILITY

The uncertainty and variability inherent in estimates of exposure and risk will be characterized regardless of the type of risk/exposure assessment conducted. Uncertainty reflects the degree of confidence in the representativeness of models or model components. Variability can be described in terms of empirical quantities that are inherently variable across time and space or between individuals (Cullen and Frey, 1999).

A tiered approach to assessing uncertainty and variability in exposure and risk estimates will be employed, beginning with a qualitative analysis and progressing to a quantitative analysis only if warranted and if data are available to support such an analysis. The first step in the uncertainty analysis would be to identify the components of the assessment, determine whether uncertainty can be evaluated for each of those components, and provide a rationale for why this is the case. The second step will be to perform a qualitative uncertainty analysis for the appropriate components of the assessment. This qualitative analysis will result in a matrix describing, for each area of uncertainty, both the magnitude (minimal, moderate, major) and the direction of influence (under- or over-estimate) on risk/exposure estimates. If sufficient data are available, and if the magnitude of uncertainty is judged significant, a quantitative assessment of uncertainty will then be performed for selected components of the assessment.

There are two primary sources of uncertainty that would be addressed in a quantitative analysis. The first is uncertainty associated with the model inputs (e.g., use of air quality data, time-location-activity diaries, microenvironmental factor distributions). The second is uncertainty associated with model formulation (e.g., simple algorithms or those incorporated in a more complex model). Each of these is generally described below using the APEX model as an example.

APEX is a Monte Carlo simulation model that explicitly incorporates the variability inherent in the model input data. A 2-dimensional Monte Carlo Latin hypercube sampling approach could be used as a combined variability and uncertainty analysis for APEX. A Monte Carlo approach entails performing a large number of model runs with inputs randomly sampled from specified distributions that reflect the variability and uncertainty of the model inputs. The 2-dimensional Monte Carlo method allows for the separate characterization of variability and uncertainty in the model results (Morgan and Henrion, 1990). If this approach were taken, developing appropriate distributions representing both variability and uncertainty in model inputs (e.g., air exchange rates, SO_2 decay rates, physiological parameters) would be a key part of the effort.

In the case of model formulation, the preferred approach would be to compare model predictions with measured values, while having relatively complete knowledge of the uncertainty associated with input parameters. For the purpose of the exposure assessment, model estimated exposures would be compared with measured personal exposures, provided appropriate data exist (e.g., similar averaging times, population demographics, geographic locations). In the absence of measurements that can be used to estimate model uncertainty, the analysis must rely on informed judgment. The approach would be to partition the model formulation uncertainty into that of the components, or sub-models, of APEX (e.g., microenvironemental concentrations, ventilation estimates). For each of the sub-models, we would discuss the simplifying assumptions and the uncertainties associated with those assumptions. Where possible, we would evaluate these sub-models by comparing their predictions with measured data. Where this is not possible, we would formulate an informed judgment regarding a range of plausible uncertainties for the sub-models.

5.7 PUBLIC AND SCIENTIFIC REVIEW

The CASAC NO_x and SO_x primary review panel will be consulted on the risk/exposure assessment scope and methods plan at a public meeting. Drafts of the risk/exposure assessment will also be reviewed by the panel. The panel will review the draft document and discuss their comments in a public meeting announced in the Federal Register. Based on CASAC's past practice, EPA expects that key CASAC advice and recommendations for revision of the document will be conveyed by the CASAC Chair in a letter to the EPA Administrator. In

revising the draft risk/exposure assessment for SO_2, EPA will take into account any such advice and recommendations. EPA will also consider comments received from CASAC or from the public at the meeting itself and any written public comments. EPA anticipates preparing a second draft of the risk/exposure assessment for CASAC review and public comment. After appropriate revision, the final document will be made available on an EPA website and subsequently printed, with its public availability being announced in the Federal Register.

6. POLICY ASSESSMENT/RULEMAKING

Based on the information in the ISA and the risk/exposure assessment report, the Agency will develop an ANPR that reflects EPA's views regarding the need to retain or revise the SO_2 NAAQS. The ANPR will identify conceptual evidence-based approaches for reaching public health policy judgments, discuss the implications for the adequacy of the current standards of the science and exposure assessments, and present exposure information associated with alternative standards. The ANPR will also describe a range of policy options for standard setting including a description of the underlying interpretations of the scientific evidence and risk/exposure information that might support such alternative standards and that could be considered by the Administrator in making NAAQS decisions.

A final decision should draw upon scientific information and analyses related to health effects, population exposure and risks, and judgments about the appropriate response to the range of uncertainties that are inherent in the scientific evidence and analyses. The Agency's approach to informing these judgments is based on a recognition that the available health effects evidence generally reflects a continuum consisting of ambient levels at which scientists generally agree that health effects are likely to occur through lower levels at which the likelihood and magnitude of the response become increasingly uncertain.

The use of an ANPR will provide an opportunity for CASAC and the public to evaluate the policy options under consideration and to offer comments and recommendations to inform the development of a proposed rule. Taking into account CASAC advice and recommendations as well as public comment on the ANPR , the Agency will publish a proposed rule, to be followed by a public comment period. Taking into account comments received on the proposed rule, the Agency will issue a final rule to complete the rulemaking process

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APPENDIX:

U.S. EPA SCIENCE ADVISORY BOARD CLEAN AIR SCIENTIFIC ADVISORY COMMITTEE MEMBERS AND THE NO_X SO_X PRIMARY STANDARD PANEL

The Clean Air Scientific Advisory Committee (CASAC) has a statutorily mandated responsibility to review and offer scientific and technical advice to the Administrator on the air quality criteria and regulatory documents that form the basis for the national ambient air quality standards (NAAQS), which currently include standards for lead (Pb), particulate matter (PM), ozone (O_3), carbon monoxide (CO), nitrogen dioxide (NO_2) and sulfur dioxide (SO_2). To perform such reviews, in each case the Committee forms a review panel consisting of CASAC members augmented by selected consultants with expertise in scientific or technical areas pertinent to the given pollutant or pollutant class under review.

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