



Integrated Review Plan for the Primary National Ambient Air Quality Standard for Sulfur Dioxide

External Review Draft

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U. S. Environmental Protection Agency

National Center for Environmental Assessment
Office of Research and Development
and
Office of Air Quality Planning and Standards
Office of Air and Radiation

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DISCLAIMER

This draft 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 standard for sulfur oxides. The approach described in this draft plan may be modified for presentation in the final plan to reflect consultation with the Clean Air Scientific Advisory Committee and public comments. Subsequent modifications to the plan may result from information developed during this review, and in consideration of advice and comments received from the Clean Air Scientific Advisory Committee and the public during the course of the review. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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LIST OF ACRONYMS/ABBREVIATIONS

AMMS	Air Monitoring and Methods Subcommittee
AQCD	Air Quality Criteria Document
AQS	EPA's Air Quality System
CAA	Clean Air Act
CASAC	Clean Air Scientific Advisory Committee
CBSA	Consolidated Business Statistical Area
CFR	Code of Federal Regulations
C-R	Concentration-response
ED	Emergency department
EPA	Environmental Protection Agency
FEM	Federal Equivalent Method
FEV ₁	Forced expiratory volume in one second, volume of air exhaled in first second of exhalation
FR	Federal Register
FRM	Federal Reference Method
HA	Hospital admissions
IRP	Integrated Review Plan
ISA	Integrated Science Assessment
Km	Kilometer
MSA	Metropolitan Statistical Area
NAAQS	National Ambient Air Quality Standards
NCEA	National Center for Environmental Assessment
NO ₂	Nitrogen dioxide
O ₃	Ozone
OAQPS	Office of Air Quality Planning and Standards
OAR	Office of Air and Radiation
OMB	Office of Management and Budget
ORD	Office of Research and Development
PA	Policy Assessment
PM	Particulate matter
ppb	Parts per billion
ppm	Parts per million
PRB	Policy-relevant background
REA	Risk and Exposure Assessment
SES	Socioeconomic status
SLAMS	State and local air monitoring stations
SO ₂	Sulfur dioxide

1. INTRODUCTION

The U.S. Environmental Protection Agency (EPA) is conducting a review of the primary (health-based) national ambient air quality standard (NAAQS) for sulfur oxides (SO_x). This draft Integrated Review Plan (IRP) presents the planned approach for the review. This review will provide an integrative assessment of relevant scientific information for SO_x and will focus on the basic elements that define the NAAQS: the indicator,¹ averaging time,² form,³ and level.⁴ The EPA Administrator will consider these elements collectively in evaluating the protection to public health afforded by the primary standard(s).

This document is organized into eight chapters. Chapter 1 presents the legislative requirements for the review of the NAAQS, background information on the review process, scope of the current review, and an overview of past reviews of the primary SO₂ NAAQS. Chapter 2 presents the status and schedule for the current review. Chapter 3 summarizes the approach in the last review and presents a set of policy-relevant questions that will serve to focus the current review on the critical scientific and policy issues. Chapters 4 through 7 discuss the planned scope and organization of key assessment documents, the planned approaches for preparing these documents, specific ambient air quality monitoring considerations, as well as plans for scientific and public review of these documents. Complete reference citations are provided in chapter 8.

1.1 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”

¹ The “indicator” of a standard defines the chemical species or mixture that is measured in determining whether an area attains the standard.

² The “averaging time” defines the time period over which ambient measurements are averaged (e.g., 1-hour, 8-hour, 24-hour, annual).

³ The “form” of a standard defines the air quality statistic that is compared to the level of the standard in determining whether an area attains the standard. For example, the form of the current 1-hour SO₂ standard is the three-year average of the 99th percentile of the annual distribution of 1-hour daily maximum SO₂ concentrations.

⁴ The “level” defines the allowable concentration of the criteria pollutant in the ambient air.

1 Section 109 (42 U.S.C. 7409) directs the Administrator to propose and promulgate
2 “primary” and “secondary” NAAQS for pollutants for which air quality criteria are issued.⁵
3 Section 109(b)(1) defines a primary standard as one “the attainment and maintenance of which in
4 the judgment of the Administrator, based on such criteria and allowing an adequate margin of
5 safety, are requisite to protect the public health.”⁶ A secondary standard, as defined in section
6 109(b)(2), must “specify a level of air quality the attainment and maintenance of which, in the
7 judgment of the Administrator, based on such criteria, is required to protect the public welfare
8 from any known or anticipated adverse effects associated with the presence of [the] pollutant in
9 the ambient air.”⁷

10 The requirement that primary standards provide an adequate margin of safety was
11 intended to address uncertainties associated with inconclusive scientific and technical
12 information available at the time of standard setting. It was also intended to provide a reasonable
13 degree of protection against hazards that research has not yet identified. See *Lead Industries*
14 *Association v. EPA*, 647 F.2d 1130, 1154 (D.C. Cir 1980), cert. denied, 449 U.S. 1042 (1980);
15 *American Petroleum Institute v. Costle*, 665 F.2d 1176, 1186 (D.C. Cir. 1981), cert. denied, 455
16 U.S. 1034 (1982). Both kinds of uncertainties are components of the risk associated with
17 pollution at levels below those at which human health effects can be said to occur with
18 reasonable scientific certainty. Thus, in selecting primary standards that include an adequate
19 margin of safety, the Administrator is seeking not only to prevent pollution levels that have been
20 demonstrated to be harmful but also to prevent lower pollutant levels that may pose an
21 unacceptable risk of harm, even if the risk is not precisely identified as to nature or degree. The
22 CAA does not require the Administrator to establish a primary NAAQS at a zero-risk level or at
23 background concentration levels, see *Lead Industries v. EPA*, 647 F.2d at 1156 n.51, *Mississippi*
24 *v. EPA*, 723 F. 3d 246, 255, 262-63 (D.C. Cir. 2013), but rather at a level that reduces risk
25 sufficiently so as to protect public health with an adequate margin of safety.

26 In addressing the requirement for an adequate margin of safety, the EPA considers such
27 factors as the nature and severity of the health effects involved, the size of the sensitive
28 population(s), and the kind and degree of uncertainties. The selection of any particular approach
29 to providing an adequate margin of safety is a policy choice left specifically to the

⁵ As discussed in section 1.4 below, this document describes the review of the *primary* SO₂ standard. The *secondary* SO₂ standard will be separately reviewed in conjunction with review of the secondary NO₂ standard.

⁶ 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)].

⁷ 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.”

1 Administrator’s judgment. See *Lead Industries Association v. EPA*, supra, 647 F.2d at 1161-62;
2 *Mississippi v. EPA*, 723 F. 3d at 265.

3 In setting standards that are “requisite” to protect public health and welfare, as provided
4 in section 109(b), the EPA’s task is to establish standards that are neither more nor less stringent
5 than necessary for these purposes. In so doing, the EPA may not consider the costs of
6 implementing the standards. See generally, *Whitman v. American Trucking Associations*, 531
7 U.S. 457, 465-472, 475-76 (2001). Likewise, “[a]ttainability and technological feasibility are not
8 relevant considerations in the promulgation of national ambient air quality standards.” *American*
9 *Petroleum Institute v. Costle*, 665 F. 2d at 1185.

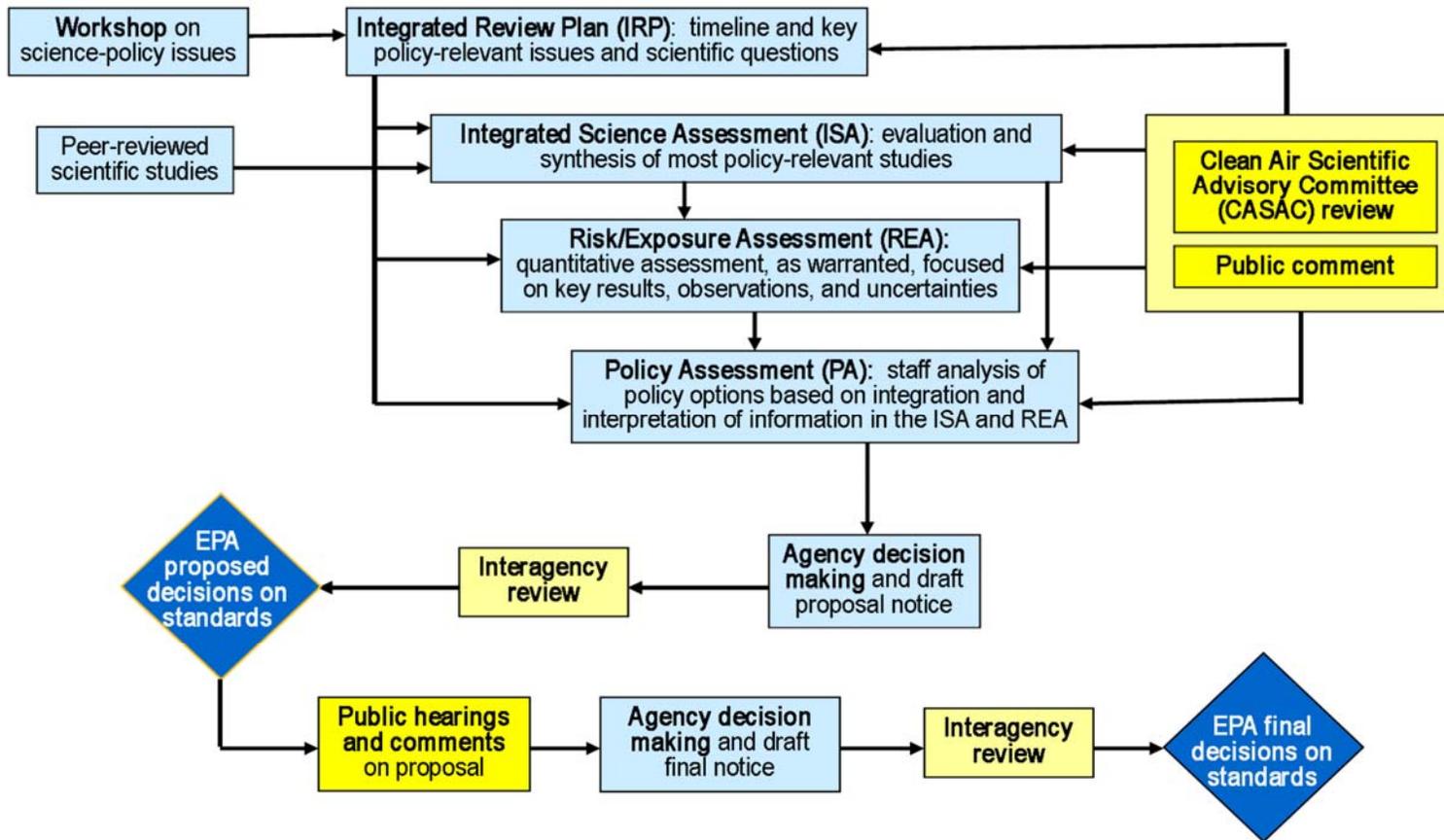
10 Section 109(d)(1) requires that “not later than December 31, 1980, and at 5-year
11 intervals thereafter, the Administrator shall complete a thorough review of the criteria
12 published under section 108 and the national ambient air quality standards . . . and shall make
13 such revisions in such criteria and standards and promulgate such new standards as may be
14 appropriate” Section 109(d)(2) requires that an independent scientific review committee
15 “shall complete a review of the criteria . . . and the national primary and secondary ambient air
16 quality standards . . . and shall recommend to the Administrator any new . . . standards and
17 revisions of existing criteria and standards as may be appropriate” Since the early 1980s,
18 this independent review function has been performed by the Clean Air Scientific Advisory
19 Committee (CASAC) of EPA’s Science Advisory Board.⁸

20 **1.2 OVERVIEW OF THE NAAQS REVIEW PROCESS**

21 The current process for reviewing the NAAQS includes four major phases: (1) planning,
22 (2) science assessment, (3) risk/exposure assessment, and (4) policy assessment and rulemaking.
23 Figure 1-1 provides an overview of this process, and each phase is described in more detail
24 below.⁹

⁸ Lists of CASAC members and of members of the CASAC Sulfur Oxides Primary NAAQS Review Panel are available at: <http://yosemite.epa.gov/sab/sabproduct.nsf/WebCASAC/CommitteesandMembership?OpenDocument>.

⁹ The EPA maintains a website on which key documents developed for NAAQS reviews are made available (<http://www.epa.gov/ttn/naaqs/>). The EPA’s NAAQS review process has evolved over time. Information on the current process is available at: <http://www.epa.gov/ttn/naaqs/review.html>. As discussed in section 1.3 below, this process was generally followed in the primary SO₂ NAAQS review completed in 2010 with the exception that there was not a separate Policy Assessment document issued; rather the Risk and Exposure Assessment (U.S. EPA 2009,) included a policy assessment chapter (i.e., Chapter 10).



1
 Figure 1-1 Overview of the NAAQS Review Process²

1 The planning phase of the NAAQS review process begins with a science policy
2 workshop, which is intended to identify issues and questions to frame the review. Drawing from
3 the workshop discussions, a draft IRP is prepared jointly by EPA's National Center for
4 Environmental Assessment (NCEA), within the Office of Research and Development (ORD),
5 and EPA's Office of Air Quality Planning and Standards (OAQPS), within the Office of Air and
6 Radiation (OAR). The draft IRP is made available for CASAC review and for public comment.
7 The final IRP is prepared in consideration of CASAC and public comments. This document
8 presents the current plan and specifies the schedule for the entire review, the process for
9 conducting the review, and the key policy-relevant science issues that will guide the review.

10 The second phase of the review, the science assessment, involves the preparation of an
11 Integrated Science Assessment (ISA) and supplementary materials. The ISA, prepared by
12 NCEA, provides a concise review, synthesis, and evaluation of the most policy-relevant science,
13 including key science judgments that are important to the design and scope of exposure and risk
14 assessments, as well as other aspects of the NAAQS review. The ISA and its supplementary
15 materials provide a comprehensive assessment of the current scientific literature pertaining to
16 known and anticipated effects on public health and welfare associated with the presence of the
17 pollutant in the ambient air, emphasizing information that has become available since the last air
18 quality criteria review in order to reflect the current state of knowledge. As such, the ISA forms
19 the scientific foundation for each NAAQS review and is intended to provide information useful
20 in forming judgments about air quality indicator(s), form(s), averaging time(s) and level(s) for
21 the NAAQS. The current review process generally includes production of a first and second
22 draft ISA, both of which undergo CASAC and public review prior to completion of the final
23 ISA. Chapter 4 below provides a more detailed description of the planned scope, organization
24 and assessment approach for the ISA and its supporting materials.

25 In the third phase, the risk/exposure assessment phase, OAQPS staff considers
26 information and conclusions presented in the ISA, with regard to support provided for the
27 development of quantitative assessments of the risks and/or exposures for health and/or welfare
28 effects. As an initial step, staff prepare a planning document (REA Planning Document) that
29 considers the extent to which newly available scientific evidence and tools/methodologies
30 warrant the conduct of quantitative risk and exposure assessments. As discussed in Chapter 5
31 below, the REA Planning Document focuses on the degree to which important uncertainties in
32 the last review may be addressed by new information available in this review. Specifically, the
33 document considers the extent to which newly available data, methods, and tools might be
34 expected to appreciably affect the assessment results, or address important gaps in our
35 understanding of the exposures and risks associated with SO₂. To the extent warranted, this
36 document outlines a general plan, including scope and methods, for conducting assessments. The

1 REA Planning Document is generally prepared in conjunction with the first draft ISA and is
2 presented for consultation with CASAC and for public comment. When an assessment is
3 performed, one or more drafts of each risk and exposure assessment document (REA) undergoes
4 CASAC and public review, with the initial draft REA generally being reviewed in conjunction
5 with review of the second draft ISA, prior to completion of the final REA. The REA provides
6 concise presentations of methods, key results, observations, and related uncertainties. Chapter 5
7 below discusses consideration of potential quantitative human health-related assessments for this
8 review.

9 The review process ends with the policy assessment and rulemaking phase. The Policy
10 Assessment (PA) is a document, prepared prior to issuance of proposed and final rules, that
11 provides a transparent presentation of OAQPS staff analysis and presents staff conclusions
12 regarding the adequacy of the current standards and, if revision is considered, what revisions
13 may be appropriate. The PA integrates and interprets the information from the ISA and REA to
14 frame policy options for consideration by the Administrator. Such an evaluation of policy
15 implications is intended to help “bridge the gap” between the Agency’s scientific assessments,
16 presented in the ISA and REA, and the judgments required of the EPA Administrator in
17 determining whether it is appropriate to retain or revise the NAAQS. In so doing, the PA is also
18 intended to facilitate CASAC’s advice to the Agency and recommendations to the Administrator
19 on the adequacy of the existing standards or revisions that may be appropriate to consider, as
20 provided for in the CAA. In evaluating the adequacy of the current standards and, as
21 appropriate, a range of alternative standards, the PA considers the available scientific evidence
22 and, as available, quantitative risk-based analyses, together with related limitations and
23 uncertainties. The PA focuses on the information that is most pertinent to evaluating the basic
24 elements of national ambient air quality standards: indicator, averaging time, form, and level.
25 One or more drafts of a PA are released for CASAC review and public comment prior to
26 completion of the final PA.

27 Following issuance of the final PA and consideration of conclusions presented therein,
28 the Agency develops and publishes a notice of proposed rulemaking that communicates the
29 Administrator’s proposed decisions regarding the standards review. A draft notice undergoes
30 interagency review involving other federal agencies prior to publication.¹⁰ Materials upon
31 which this decision is based, including the documents described above, are made available to the

¹⁰ Where implementation of the proposed decision would have an annual effect on the economy of \$100 million or more, e.g., by necessitating the implementation of emissions controls, the EPA develops and releases a draft regulatory impact analysis (RIA) concurrent with the notice of proposed rulemaking. This activity is conducted under Executive Order 12866. The RIA is conducted completely independent of and, by statute, is not considered in decisions regarding the review of the NAAQS.

1 public in the regulatory docket for the review.¹¹ A public comment period, during which public
2 hearings are generally held, follows publication of the notice of proposed rulemaking. Taking
3 into account comments received on the proposed rule,¹² the Agency develops a final rule which
4 undergoes interagency review prior to publication to complete the rulemaking process. Chapter
5 7 discusses the development of the PA and the rulemaking steps for this review.
6

7 **1.3 HISTORY OF THE REVIEW OF AIR QUALITY CRITERIA FOR** 8 **SULFUR OXIDES AND THE NAAQS FOR SULFUR DIOXIDE**

9 The EPA completed the initial review of the air quality criteria for sulfur oxides in 1969
10 (34 FR 1988). Based on this review, the EPA in initially promulgating NAAQS for sulfur oxides
11 in 1971, established the indicator as SO₂. The 1971 primary standards were set at 0.14 parts per
12 million (ppm) averaged over a 24-hour period, not to be exceeded more than once per year, and
13 0.030 ppm annual arithmetic mean.¹³ Since then, the Agency has completed multiple reviews of
14 the air quality criteria and standards, as summarized in Table 1-1.
15

¹¹ All documents in the docket are listed in the www.regulations.gov index. Publicly available docket materials are available either electronically at www.regulations.gov or in hard copy at the Air and Radiation Docket and Information Center. The docket ID number for this review is EPA-HQ-OAR-2013-0566.

¹² When issuing the final rulemaking, the Agency responds to all significant comments on the proposed rule.

¹³ Note that 0.14 ppm is equivalent to 140 parts per billion (ppb) and 0.030 ppm is equivalent to 30 ppb.

Table 1-1. History of the primary national ambient air quality standard(s) for sulfur dioxide since 1971¹⁴

Final Rule/Decision	Indicator	Averaging Time	Level	Form
1971 36 FR at 8186 Apr 30, 1971	SO ₂	24-hour and Annual Avg	24-hour: 140 ppb Annual Avg: 30 ppb ¹⁵	24-hour std: one allowable exceedance Annual std: Annual arithmetic average
1996 61 FR at 25566 May 22, 1996	Both the 24-hour and annual average standards retained without revision			
2010 75 FR at 35520 June 22, 2010	SO ₂	1-hour	75 ppb	99 th percentile, averaged over 3 years ¹⁶
	24-hour and annual SO ₂ standards revoked.			

In 1982, the EPA published the *Air Quality Criteria for Particulate Matter and Sulfur Oxides* (U.S. 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 (U.S. EPA 1982). In 1986, a second addendum was published presenting newly available evidence from epidemiologic and controlled human exposure studies (U.S. EPA 1986). In 1988, the EPA published a proposed decision not to revise the existing standards (53 FR 14926). However, the 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 to protect against short-term peak exposures.

As a result of public comments on the 1988 proposal and other post-proposal developments, the 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 SO₂ exposures in asthmatics (U.S. EPA 1994). As in the 1988 proposal, the 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 SO₂ if additional protection were judged

¹⁴ In 1971 (36 FR 8186), a 3-hour secondary standard was set at 500 ppb to provide protection against adverse welfare effects.

¹⁵ The initial level of the 24-hr SO₂ standard was 0.140 ppm which is equal to 140 ppb. The initial level of the annual SO₂ standard was 0.03 ppm which is equal to 30 ppb.

¹⁶ The form of the 1-hour standard is the 3-year average of the 99th percentile of the yearly distribution of 1-hour daily maximum SO₂ concentrations.

1 to be necessary. The three alternatives were: 1) Revising the existing primary SO₂ NAAQS by
2 adding a new 5-minute standard of 0.60 ppm SO₂; 2) establishing a new regulatory program
3 under section 303 of the Act to supplement protection provided by the existing NAAQS, with a
4 trigger level of 0.60 ppm SO₂, one expected exceedance; and 3) augmenting implementation of
5 existing standards by focusing on those sources or source types likely to produce high 5-minute
6 peak concentrations of SO₂.

7 In assessing the regulatory options mentioned above, the Administrator concluded that
8 the likely frequency of 5-minute concentrations of concern should also be a consideration in
9 assessing the overall public health risks. Based upon an exposure analysis conducted by the
10 EPA, the Administrator concluded that exposure of asthmatics to SO₂ at levels that can reliably
11 elicit adverse health effects was likely to be a rare event when viewed in the context of the entire
12 population of asthmatics. As a result, the Administrator judged that 5-minute peak SO₂ levels
13 did not pose a broad public health problem when viewed from a national perspective, and a 5-
14 minute standard was not promulgated. In addition, no other regulatory alternative was finalized
15 and the 24-hour and annual average primary SO₂ standards were retained in 1996 (61 FR 25566).

16 The American Lung Association and the Environmental Defense Fund challenged EPA's
17 decision not to establish a 5-minute standard. On January 30, 1998, the Court of Appeals for the
18 District of Columbia found that the EPA had failed to adequately explain its determination that
19 no revision to the SO₂ NAAQS was appropriate and remanded the decision back to EPA for
20 further explanation. Specifically, the court required the EPA to provide additional rationale to
21 support the Agency judgment that 5-minute peaks of SO₂ do not pose a public health problem
22 from a national perspective even though these peaks will likely cause adverse health impacts in a
23 subset of asthmatics. In response, the EPA collected and analyzed additional air quality data
24 focused on 5-minute concentrations of SO₂ and used this information to inform the last review of
25 the SO₂ NAAQS.

26 On June 22, 2010, the EPA revised the primary SO₂ NAAQS to provide requisite
27 protection of public health with an adequate margin of safety. Specifically, after concluding that
28 the then-existing 24-hour and annual standards were inadequate to protect public health with an
29 adequate margin of safety (see section 3.1.1), the EPA established a new 1-hour SO₂ standard at
30 a level of 75 ppb, based on the 3-year average of the annual 99th percentile of 1-hour daily
31 maximum concentrations (see section 3.1.2). This standard was promulgated to provide
32 substantial protection against SO₂-related health effects associated with short-term exposures
33 ranging from 5-minutes to 24-hours. More specifically, EPA concluded that a 1-hour SO₂
34 standard at 75 ppb would provide substantial protection against the adverse respiratory effects
35 (e.g., decrements in lung function and/or respiratory symptoms) reported in exercising asthmatics
36 following 5-10 minute exposures in controlled human exposure studies, as well as the more

1 serious health associations reported in epidemiologic studies of mostly 1- and 24-hours (e.g.,
2 respiratory-related emergency department visits and hospitalizations). In the last review, the
3 EPA also revoked the then-existing 24-hour and annual primary standards because neither of
4 these standards would likely provide additional public health protection given a 1-hour standard
5 at 75 ppb (see section 3.1.2). The decision to set a 1-hour standard at 75 ppb to in part, provide
6 substantial protection against 5- minute concentrations of SO₂ resulting in adverse respiratory
7 effects in exercising asthmatics, also satisfied the DC Circuit Court remand of 1996.

8 As mentioned above, in the last review substantial weight was placed on preventing
9 health effects associated with 5-minute peak SO₂ concentrations. Thus, as part of the final
10 rulemaking, the EPA for the first time required state reporting of either the highest 5-minute
11 concentration for each hour of the day, or all twelve 5-minute concentrations for each hour of the
12 day (see chapter 6). The rationale for this requirement was that this additional monitored data
13 could then be used in future reviews to evaluate the extent to which the 1-hour SO₂ NAAQS at
14 75 ppb provides protection against 5-minute peaks of concern.

15 After publication of the final rule, a number of industry groups and states filed petitions
16 for review maintaining that the 1-hour SO₂ NAAQS at 75 ppb was overly stringent or otherwise
17 arbitrary. The D.C. Circuit rejected these challenges, upholding the standard in its entirety.
18 *National Environmental Development Association's Clean Air Project v. EPA*, 686 F. 3d 803
19 (D.C. Cir. 2012).

21 **1.4 SCOPE OF THE CURRENT REVIEW**

22 Sulfur oxides include all forms of oxidized sulfur compounds including the gases SO₂
23 and SO₃ as well as their gaseous and particulate reaction products (e.g., sulfates; see 34 FR
24 1988). As in previous reviews of the SO₂ NAAQS, this review will focus on effects associated
25 with the gaseous species only. Effects associated with the particulate species (e.g., sulfate) are
26 addressed in the review of the NAAQS for particulate matter (PM) (78 FR 30866, January 15,
27 2013; U.S. EPA 2009).

28 Consistent with the review completed in 2010, this review is focused on the primary SO₂
29 standard and as such, will only consider relevant scientific information related to potential health
30 effects associated with exposure to sulfur oxides. The EPA is separately reviewing the
31 secondary SO₂ standard in conjunction with a review of the secondary NO₂ standard (78 FR
32 53452, August 29, 2013).¹⁷

¹⁷ Additional information on the ongoing review of the secondary NO₂ and SO₂ standards is available at:
<http://www.epa.gov/ttn/naaqs/standards/no2so2sec/index.html>.

2. STATUS AND SCHEDULE

In May of 2013, the EPA announced the initiation of the current periodic review of the air quality criteria for SO_x and the primary SO₂ NAAQS, and also issued a call for information in the *Federal Register* (78 FR 27387). Also, as an initial step in the NAAQS review process described in Section 1.1 above, EPA invited a wide range of external and internal EPA experts, representing a variety of areas of expertise (e.g., epidemiology, human and animal toxicology, statistics, risk/exposure analysis, atmospheric science), to participate in a workshop to discuss the policy-relevant science to inform development of this plan. This workshop was held June 12-13, 2013, in Research Triangle Park, NC (78 FR 27387). This workshop provided an opportunity for the participants to broadly discuss the key policy-relevant issues around which EPA would structure the SO₂ NAAQS review and to discuss the most meaningful new science that would be available to inform our understanding of these issues. Based in part on the workshop discussions, the EPA developed this draft IRP outlining the schedule, the process, and the policy-relevant science issues identified as key to guiding the evaluation of the air quality criteria for sulfur oxides and the review of the primary SO₂ NAAQS.

Table 2-1 outlines the schedule under which the Agency is currently conducting this review. The scope of the review and the key documents to be prepared during the review are discussed throughout the rest of this document.

Table 2-1. Anticipated schedule for the SO₂ NAAQS Review

Stage of Review	Major Milestone	Draft Target Date
Integrated Plan (IRP)	Literature Search	Ongoing
	Call for Information	May 10, 2013
	Workshop on science/policy issues	June 12-13 2013
	Draft IRP	March 2014
	CASAC/public review on draft IRP	April 22, 2014
	Final IRP	July 2014
Integrated Science Assessment (ISA)	First draft ISA	October 2014
	CASAC/public review first draft ISA	January 2015
	Second draft ISA	July 2015
	CASAC/public review second draft ISA	October 2015
	Final ISA	January 2016
Risk/Exposure Assessment (REA)	REA Planning Document	February 2015
	CASAC consultation/public review REA Planning Document	March 2015
	If warranted:	
	First draft REA	¹⁸
	CASAC/public review of first draft REA	
	Second draft REA	
	CASAC/public review of second draft REA	
	Final REA	
Policy Assessment (PA)/Rulemaking	First Draft PA	September 2015
	CASAC review/public review first draft PA	October 2015
	Second Draft PA (if warranted)	June 2016
	CASAC/public review second draft PA	July 2016 ¹⁹
	Final PA	December 2016
	Notice of proposed rulemaking	May 2017
	Notice of final rulemaking	February 2018

¹⁸ An updated REA may not be warranted for the reviews of the SO₂ primary NAAQS

¹⁹ The anticipated schedule presented in Table 2-1 includes preparation of two draft PAs for CASAC and public review. In NAAQS reviews in which the newly available information calls into question the adequacy of the current standard(s), a second draft PA is typically prepared to include staff consideration of potential alternative standards. However, in NAAQS reviews where a new REA is not developed and where staff preliminarily conclude in a first draft PA that it is appropriate to consider retaining the current standards without revision, the EPA may decide that there is no new substantive information that we would intend to add that would provide a basis for preparing a second draft PA. If the Agency determines that a second draft PA is not warranted, CASAC and public comments on the first draft PA will be considered in preparing the final PA and the schedule for the review will be revised accordingly.

3. KEY POLICY-RELEVANT ISSUES

The overarching question in each NAAQS review is:

- **Does the currently available scientific evidence and exposure/risk-based information support or call into question the adequacy of the protection afforded by the current standard(s)?**

As appropriate, a review also addresses a second overarching question:

- **What alternative standard(s), if any, are supported by the currently available scientific evidence and exposure/risk-based information and are appropriate for consideration?**

To inform our consideration of these overarching questions in the current review, we have identified key policy-relevant issues to be considered. These key issues reflect aspects of the health effects evidence, air quality information, and exposure/risk information that, in our judgment, are likely to be particularly important to informing the Administrator's decisions. They build upon the key issues that were important in previous reviews.

Section 3.1 below describes the key considerations and conclusions from the last review with regard to the adequacy of the then-current primary SO₂ standards (section 3.1.1), and with regard to the elements for a revised standard judged in that review to provide requisite public health protection (section 3.1.2). Section 3.2 summarizes our general approach for reviewing the primary SO₂ standard in the current review and outlines the key policy-relevant issues. These issues are presented as a series of questions that will frame our approach to considering the extent to which the available evidence and information support retaining or revising the current primary standard for SO₂.

3.1 CONSIDERATIONS AND CONCLUSIONS IN LAST REVIEW

The last review of the primary NAAQS for SO₂ was completed in 2010 (75 FR at 35520, June 22, 2010). In that review, the EPA considered key controlled human exposure studies from previous reviews as well as the significantly expanded body of health effects evidence that had emerged since the last review was completed in 1996.²⁰ In addition, EPA also considered exposure and risk estimates regarding potential respiratory effects in exercising asthmatics following 5-10 minute exposures to SO₂, as well as CASAC advice and public comments. Taking all this information together, the EPA established a new short-term standard to provide

²⁰ Documents related to the SO₂ NAAQS reviews completed in 2010 and 1996 are available at: http://www.epa.gov/ttn/naaqs/standards/so2/s_so2_index.html

1 increased protection for asthmatics and other at-risk populations²¹ against an array of adverse
2 respiratory effects that have been linked to short-term SO₂ exposures in both controlled human
3 exposure and epidemiologic studies (75 FR at 35525 to 35527 and U.S. EPA 2008, section 5.5).
4 Specifically, the EPA established a short-term standard defined by the 3-year average of the 99th
5 percentile of the yearly distribution of 1-hour daily maximum SO₂ concentrations, with a level of
6 75 ppb. In addition to setting a new short-term standard, the then-existing 24-hour and annual
7 standards were revoked based largely on the recognition that a 1-hour standard set at 75 ppb
8 would have the effect of generally maintaining 24-hour and annual SO₂ concentrations well
9 below the levels of those standards (75 FR at 35550).

10 Key policy-relevant aspects of the Administrator’s decisions with regard to the need to
11 revise the primary SO₂ NAAQS, and with regard to the elements of the revised standard, are
12 described below in sections 3.1.1 and 3.1.2, respectively. Areas of uncertainty identified in the
13 last review are noted in section 3.1.3.
14

15 **3.1.1 Need for Revision**

16 The Administrator concluded in the last review that the then-existing 24-hour and annual
17 SO₂ standards were not adequate to protect public health, including the health of at-risk
18 populations, from the effects associated with short-term exposures to SO₂ (75 FR at 35520, June
19 22, 2010). As described below, this conclusion was based on the extensive body of health
20 evidence assessed in the 2008 ISA (U.S. EPA 2008), including the assessment of the policy-
21 relevant aspects of that evidence,²² quantitative exposure and risk analyses presented in the 2009
22 REA (U.S. EPA 2009), public comments, and the advice and recommendations of CASAC
23 (Samet, 2009).

24 As an initial consideration in reaching this conclusion, the Administrator noted the ISA
25 judgement that the findings of controlled human exposure, epidemiologic, and animal
26 toxicological studies collectively provided evidence “sufficient to infer a causal relationship”
27 between short-term SO₂ exposures ranging from 5-minutes to 24-hours and respiratory morbidity
28 (75 FR at 35535). The ISA described the “definitive evidence” for this conclusion as being the
29 results of 5–10 minute controlled human exposure studies demonstrating decrements in lung

²¹ As used here and similarly throughout this document, the term *population* refers to persons having a quality or characteristic in common, such as a specific pre-existing illness or a specific age or lifestage. A lifestage refers to a distinguishable time frame in an individual’s life characterized by unique and relatively stable behavioral and/or physiological characteristics that are associated with development and growth. Identifying at-risk populations includes consideration of intrinsic (e.g., genetic or developmental aspects) or acquired (e.g., disease or smoking status) factors that increase the risk of health effects occurring with exposure to sulfur oxides as well as extrinsic, nonbiological factors such as those related to socioeconomic status, reduced access to health care, or exposure.

²² As noted in section 1.3 above, due to changes in the NAAQS process, the last review of the SO₂ NAAQS did not include a separate Policy Assessment. Rather, the REA for that review included a Policy Assessment chapter.

1 function and/or respiratory symptoms in exercising asthmatics (U.S. EPA 2008, section 5.2). In
2 brief, the ISA examined numerous controlled human exposure studies and found that moderate
3 or greater decrements in lung function (i.e., $\geq 15\%$ decline in Forced Expiratory Volume (FEV₁)
4 and/or $\geq 100\%$ increase in specific airway resistance (sRaw)) occurred in some exercising
5 asthmatics exposed to SO₂ concentrations as low as 200–300 ppb for 5–10 minutes. The ISA also
6 found that among asthmatics, both the percentage of individuals affected, and the severity of the
7 response increased with increasing SO₂ concentrations. That is, at 5–10 minute concentrations
8 ranging from 200–300 ppb, the lowest levels tested in free breathing chamber studies,
9 approximately 5–30% percent of exercising asthmatics experienced moderate or greater
10 decrements in lung function (U.S. EPA 2008, Table 3–1). At concentrations of 400–600 ppb,
11 moderate or greater decrements in lung function occurred in approximately 20– 60% of
12 exercising asthmatics, and compared to exposures at 200–300 ppb, a larger percentage of
13 asthmatics experienced severe decrements in lung function (i.e., $\geq 20\%$ decrease in FEV₁ and/or
14 $\geq 200\%$ increase in sRaw; U.S. EPA 2008, Table 3–1). Moreover, at SO₂ concentrations ≥ 400
15 ppb, moderate or greater decrements in lung function were often statistically significant at the
16 group mean level and were frequently accompanied by respiratory symptoms (U.S. EPA 2008,
17 Table 3–1).

18 In considering the controlled human exposure studies with respect to adequacy of the
19 then-current standards, the Administrator first judged that 5–10 minute SO₂ exposures ≥ 400 ppb
20 and ≥ 200 ppb can result in adverse health effects in exercising asthmatics (75 FR at 35536).
21 This judgment was based on ATS guidelines, explicit CASAC consensus written advice, as well
22 as recommendations and judgments made by EPA in previous NAAQS reviews (see 75 FR at
23 35526 and 75 FR at 35536). The Administrator therefore particularly noted analyses in the REA
24 that utilized benchmark concentrations derived from the controlled human exposure evidence. In
25 the REA, 5-minute benchmark concentrations ranged from 100 ppb to 400 ppb (see below,
26 section 5.1), with 5-minute benchmark concentrations of 200 ppb and 400 ppb noted by the
27 Administrator as being particularly important. These benchmark levels were highlighted because
28 in free-breathing controlled human exposure studies: (1) 400 ppb represented the lowest
29 concentration at which moderate or greater lung function decrements occurred which were often
30 statistically significant at the group mean level and were frequently accompanied by respiratory
31 symptoms; and (2) 200 ppb was the lowest level at which moderate or greater decrements in lung
32 function were found in some individuals.²³

33 Given the emphasis on the 200 ppb and 400 ppb benchmarks, the Administrator
34 particularly noted the modeled exposure analysis results for the St. Louis case study presented in

²³ 200 ppb was also the lowest level tested in free-breathing controlled human exposure studies.

1 the REA (see below, section 5.1). This analysis estimated that given air quality simulated to just
2 meet the then-existing SO₂ NAAQS, substantial percentages of asthmatic children at moderate or
3 greater exertion would be exposed, at least once annually, to air quality exceeding the 200 ppb
4 and 400 ppb 5-minute benchmarks (75 FR at 35536). The Administrator judged these 5-minute
5 exposures to be significant from a public health perspective due to their estimated frequency:
6 approximately 24% of asthmatic children at moderate or greater exertion in St. Louis were
7 estimated to be exposed at least once per year to air quality exceeding the 5- minute 400 ppb
8 benchmark. Additionally, approximately 73% of asthmatic children in St. Louis at moderate or
9 greater exertion were estimated to be exposed at least once per year to air quality exceeding the
10 5-minute 200 ppb benchmark (75 FR at 35536).

11 With respect to the epidemiologic evidence, the ISA characterized epidemiologic studies
12 of respiratory symptoms, emergency department visits and hospital admissions as providing
13 “supporting evidence” for the causal relationship between short-term exposure to SO₂ and
14 respiratory morbidity. The ISA found that numerous epidemiologic studies reported positive
15 associations between ambient SO₂ concentrations and respiratory symptoms in children, as well
16 as emergency department visits and hospitalizations for all respiratory causes and asthma across
17 multiple age groups. The ISA concluded that these epidemiologic studies were consistent and
18 coherent. This evidence was consistent in that associations were reported in studies conducted in
19 numerous locations and with a variety of methodological approaches (U.S. EPA 2008, section
20 5.2). It was coherent in that respiratory symptom results from epidemiologic studies of short-
21 term (predominantly 1-hour daily maximum or 24-hour average) SO₂ concentrations were
22 generally in agreement with respiratory symptom results from controlled human exposure studies
23 of 5–10 minutes. Moreover, while recognizing the uncertainties associated with separating the
24 effects of SO₂ from those of co-occurring pollutants, the ISA concluded that “the limited
25 available evidence indicates that the effect of SO₂ on respiratory health outcomes appears to be
26 generally robust and independent of the effects of gaseous co-pollutants, including NO₂ and O₃,
27 as well as particulate copollutants, particularly PM_{2.5}” (U.S. EPA 2008, section 5.3).

28 In considering the epidemiologic evidence, the Administrator acknowledged uncertainties
29 with these studies (e.g., potential confounding by co-pollutants), but agreed with judgments in
30 the ISA that the epidemiologic evidence, supported by the controlled human exposure evidence,
31 generally indicated that the effects seen in these studies were attributable to exposure to SO₂,
32 rather than co-pollutants. With respect to the adequacy of the SO₂ NAAQS, the Administrator
33 noted that many of these epidemiologic studies reported associations between short-term (mostly
34 1-hour daily maximum and 24-hour average) SO₂ concentrations and respiratory symptoms,
35 emergency department visits, and hospital admissions in locations meeting the then-existing 24-

1 hour and annual standards (75 FR at 35535), thereby further indicating that the these standards
2 were not adequately protecting public health.

3 The Administrator also agreed with specific CASAC advice when reaching the decision
4 that the then-existing standards were not adequate to protect public health with an adequate
5 margin of safety. Specifically, CASAC advised that: “the current 24-hour and annual standards
6 are not adequate to protect public health, especially in relation to short-term exposures to SO₂
7 (5–10 minutes) by exercising asthmatics” (Samet, 2009, p. 15).

8 Based on the considerations summarized above, the Administrator concluded that the
9 then-existing 24-hour and annual primary SO₂ NAAQS were not adequate to protect public
10 health with an adequate margin of safety and that these standards should be revised in order to
11 provide increased public health protection against respiratory effects associated with short-term
12 exposures, particularly for susceptible populations such as asthmatics and children. Upon
13 consideration of approaches to revising these standards, the Administrator concluded that it was
14 appropriate to set a new short-term standard, as described below.

15 **3.1.2 Elements of a Revised Standard**

16 When considering alternative standards to provide requisite public health protection, the
17 Administrator concluded it was appropriate to set a new 1-hour SO₂ standard at a level of 75 ppb,
18 based on the 3-year average of the 99th percentile of the yearly distribution of 1-hour daily
19 maximum concentrations. The rationale and approach for setting the 1-hour standard is
20 presented below in terms of the individual elements of a NAAQS: indicator, averaging time,
21 form, and level. Notably, given a new 1-hour standard at 75 ppb, the previous 24-hour and
22 annual standards were revoked because neither of these standards was likely to provide
23 additional public health protection (74 FR at 35550).

24 **Indicator**

25 In previous reviews, the EPA focused on SO₂ as the most appropriate indicator for sulfur
26 oxides because the available scientific information regarding health effects was overwhelmingly
27 indexed by SO₂. In the most recent review, this continued to be the case. Controlled human
28 exposure studies and animal toxicological studies provided specific evidence for health effects
29 following exposures to SO₂. In addition, epidemiologic studies typically reported effects
30 associated with SO₂ concentrations. Thus, based on the information available in the last review
31 and consistent with the views of CASAC that: “for indicator, SO₂ is clearly the preferred
32 choice” (Samet 2009, p. 14), the Administrator concluded it was appropriate to continue to use
33 SO₂ as the indicator for a standard that was intended to address effects associated with exposure
34 to SO₂, alone or in combination with other gaseous sulfur oxides (75 FR at 35536). In so doing,
35 the EPA recognized that measures leading to reductions in population exposures to SO₂ will also
36 likely reduce exposures to other sulfur oxides (75 FR at 35536).

1 **Averaging Time**

2 When considering the level of support available for specific averaging times, the
3 Administrator first considered the strength of evidence from controlled human exposure and
4 epidemiologic studies. As noted above (see section 3.1.1), controlled human exposure studies
5 exposed exercising asthmatics to SO₂ for 5 -10 minutes and consistently found decrements in
6 lung function and/or respiratory symptoms. Importantly, the ISA described the controlled human
7 exposure studies as being the “definitive evidence” for its conclusion that there existed a causal
8 relationship between short-term (5-minutes to 24-hours) SO₂ exposure and respiratory morbidity
9 (U.S. EPA 2008, section 5.2). Supporting the controlled human exposure evidence were
10 epidemiologic studies describing positive associations between short-term (e.g., 1-hour daily
11 maximum and 24-hour average) SO₂ levels and respiratory symptoms as well as hospital
12 admissions and emergency department visits for all respiratory causes and asthma (U.S. EPA
13 2008, Tables 5.4 and 5.5). Taken together, it was judged that controlled human exposure studies
14 provided support for an averaging time that protected against 5-10 minute peak exposures, while
15 epidemiologic evidence provided support for an averaging time that protected against both 1-
16 hour and 24-hour exposures (U.S. EPA 2009, section 10.5.2.1).²⁴

17 In further considering an appropriate averaging time, the Administrator took into account
18 air quality analyses from the REA examining the potential for 24-hour and 1-hour averaging
19 times to protect against 5-minute peak concentrations. Results of these analyses suggested that a
20 standard based on 24-hour average SO₂ concentrations would not likely be an effective or
21 efficient approach for addressing 5-minute peak SO₂ concentrations. That is, using a 24-hour
22 average standard to address 5-minute peaks would likely result in over-controlling in some areas,
23 while under-controlling in others (U.S. EPA 2009, section 10.5.2.2). In contrast, these analyses
24 suggested that a standard with a 1-hour averaging time would be more efficient and effective at
25 limiting 5-minute peaks of SO₂ (U.S. EPA 2009, section 10.5.2.2). In additional air quality
26 analyses, the REA suggested that a 1-hour standard (given an appropriate form and level) could
27 likely provide protection against 99th percentile 1-hour daily maximum and 99th percentile 24-
28 hour average SO₂ concentrations found in locations where emergency department visit and
29 hospital admission studies using multi-pollutant models with PM reported statistically significant
30 associations with ambient SO₂ (75 FR at 35539 and U.S. EPA 2009, section 10.5.2.2).²⁵
31 Considering this information, the Administrator concluded that a 1-hour standard (given an

²⁴ The ISA did note that effects observed in epidemiologic studies also may have been due, at least in part, and especially in 24-hour epidemiologic studies, to shorter-term peaks of SO₂ (see U.S. EPA 2008, section 5.2). More specifically, the ISA noted “that it is possible that these associations are determined in large part by peak exposures within a 24-hour period” (U.S. EPA 2008, section 5.2).

²⁵ Since SO₂ is a pre-cursor to PM (e.g., sulfates), there was special consideration given to epidemiologic studies that used multipollutant models to separate the estimated SO₂ associations from that of PM.

1 appropriate form and level) was an appropriate means of controlling short-term exposures to SO₂
2 ranging from 5-minutes to 24-hours (74 FR at 35539).

3 The Administrator further noted that establishing a 1-hour averaging time was in
4 agreement with CASAC recommendations (74 FR at 35539). That is, CASAC stated that they
5 were “in agreement with having a short-term standard and finds that the REA supports a one-
6 hour standard as protective of public health” (Samet 2009, p. 1). CASAC also stated that a
7 “one-hour standard is the preferred averaging time” (Samet 2009, p.15).

8 Based solely on the controlled human exposure evidence, the Administrator also
9 considered a 5-minute averaging time in the last review. However, such an approach was not
10 favored. With respect to a 5-minute standard, there were concerns about standard stability.
11 Specific concerns related to the number of monitors needed and the placement of such monitors
12 given the temporal and spatial heterogeneity of 5-minute SO₂ concentrations (74 FR at 35539).
13 However, as noted above, the Administrator judged that a 1-hour averaging time, given an
14 appropriate form and level, could adequately limit 5-minute SO₂ exposures and provide a more
15 stable regulatory target than setting a 5-minute standard. Consequently, the Administrator judged
16 that a 5-minute averaging time was not the preferred approach to provide adequate public health
17 protection (74 FR at 35539).

18 **Form**

19 The “form” of a standard defines the air quality statistic that is to be compared to the
20 level of the standard in determining whether an area attains the NAAQS. In the last review,
21 controlled human exposure evidence presented in the ISA indicated that the percentage of
22 asthmatics affected and the severity of the response increased with increasing SO₂
23 concentrations. Thus, a concentration-based form averaged over three years was judged by the
24 Administrator to be most appropriate (74 FR at 35541). This was because compared to an
25 exceedance-based form, a concentration-based form averaged over three years would give more
26 weight to years when 1-hour SO₂ concentrations are well above the level of the standard, than to
27 years when 1- hour SO₂ concentrations are just above the level of the standard. The
28 Administrator also noted that a concentration-based form averaged over 3 years would likely be
29 appreciably more stable than a no exceedance-based form (75 FR at 35541). Establishing a
30 concentration-based form was also in agreement with specific CASAC advice stating that “there
31 is adequate information to justify the use of a concentration-based form averaged over 3 years”
32 (Samet 2009, p. 16)

33 In selecting a specific concentration-based form, the Administrator considered health
34 evidence from the ISA as well as air quality and exposure information from the REA. In the ISA,
35 it was noted that a few epidemiologic studies reported an increase in SO₂-related respiratory
36 health effects at the upper end of the distribution of ambient SO₂ concentrations (i.e., above 90th

1 percentile SO₂ concentrations; see U.S. EPA 2008, section 5.3). In the REA, air quality and
2 exposure analyses suggested that a 99th percentile form was likely to be appreciably more
3 effective at limiting 5-minute peak exposures of concern than a 98th percentile form (at a given
4 standard level; U.S. EPA 2009, section 10.5.3, and U.S. EPA 2009, Figures 7–27 and 7–28).
5 Taken together, the Administrator concluded that a 99th percentile form (at an appropriate level)
6 would limit both the upper end of the distribution of ambient SO₂ concentrations reported in
7 some epidemiologic studies to be associated with increased risk of SO₂-related respiratory
8 morbidity effects (e.g., emergency department visits), as well as 5-minute peak SO₂
9 concentrations resulting in decrements in lung function and/or respiratory symptoms in
10 controlled human exposure studies (75 FR at 35541).

11 **Level**

12 Controlled human exposure evidence was described in the ISA as providing the definitive
13 evidence for a causal association between short-term exposure to SO₂ and respiratory morbidity.
14 The Administrator therefore placed considerable emphasis on these studies when selecting the
15 level of a new 1-hour standard. In particular, the Administrator wanted the level of a 1-hour
16 standard to provide substantial protection against the 200 ppb and 400 ppb 5-minute benchmarks
17 identified from these studies. As noted above (see section 3.1.1), these benchmark levels were
18 highlighted because in free-breathing controlled human exposure studies of exercising
19 asthmatics: (1) 400 ppb represented the lowest concentration where moderate or greater lung
20 function decrements occurred which were often statistically significant at the group mean level
21 and were frequently accompanied by respiratory symptoms; and (2) 200 ppb was the lowest level
22 at which moderate or greater decrements in lung function were found in some asthmatics.²⁶

23 Analyses in the REA described the varying degrees of protection different 1-hour
24 standard levels could provide against 5-minute benchmark concentrations of 200 ppb and 400
25 ppb (see below section 5.1). Considering these analyses, the Administrator judged that a 1-hour
26 standard level of 100 ppb would appropriately limit the occurrence of 5-minute benchmark
27 concentrations \geq 200 or 400 ppb (74 FR at 35547). That is, the St. Louis exposure simulation
28 estimated that a 1-hour standard at 100 ppb would likely protect $>$ 99% of asthmatic children in
29 that city at moderate or greater exertion from experiencing at least one 5-minute exposure \geq 400
30 ppb per year, and approximately 97% of those asthmatic children at moderate or greater exertion
31 from experiencing at least one exposure \geq 200 ppb per year (74 FR at 35547). Moreover, the
32 40-county air quality analysis from the REA (see below section 5.1) estimated that a 100 ppb 1-
33 hour standard would allow at most 2 days per year on average in any county when estimated 5-
34 minute daily maximum SO₂ concentrations exceed the 400 ppb benchmark, and at most 13 days

²⁶ As noted in section 3.1.1, 200 ppb was also the lowest level tested in free-breathing controlled human exposure studies.

1 per year on average when 5-minute daily maximum SO₂ concentrations exceed the 200 ppb
2 benchmark²⁷ (74 FR at 35546). Furthermore, given a simulated 1-hour 100 ppb standard level,
3 most of the counties in that air quality analysis were estimated to experience 0 days per year on
4 average when 5-minute daily maximum SO₂ concentrations exceed the 400 ppb benchmark and
5 ≤ 3 days per year on average when 5-minute daily maximum SO₂ concentrations were estimated
6 to exceed the 200 ppb benchmark (74 FR at 35546).

7 In considering the epidemiologic evidence with respect to level, the Administrator noted
8 that there were more than 50 peer-reviewed epidemiologic studies published worldwide
9 evaluating SO₂ since the prior review (75 FR at 35547). The Administrator also noted that these
10 studies generally reported positive, although not always statistically significant associations
11 between more serious health outcomes (i.e. respiratory-related emergency department visits and
12 hospitalizations) and ambient SO₂ concentrations (75 FR at 35547). She further agreed with the
13 ISA finding that the controlled human exposure evidence lends biological plausibility to the
14 effects reported in epidemiologic studies (75 FR at 35547), and that when evaluated as a whole,
15 the results of epidemiologic studies were generally independent of the effects of gaseous and
16 particulate co-pollutants (74 FR at 35544 and 75 FR 35547). Taken together, the Administrator
17 judged it appropriate to place emphasis on the epidemiologic evidence when further considering
18 the appropriate level of a new 1-hour standard.

19 In considering the epidemiologic evidence with respect to level, the Administrator placed
20 primary emphasis on ten U.S. epidemiologic studies (some conducted in multiple locations)
21 reporting mostly positive and sometimes statistically significant associations between ambient
22 SO₂ concentrations and emergency department visit and hospital admissions in locations where
23 99th percentile 1-hour daily maximum SO₂ levels ranged from approximately 50–460 ppb (74 FR
24 at 35547). The Administrator further noted that within this broader range of SO₂ concentrations
25 there was a cluster of three epidemiologic studies between 78–150 ppb (for the 99th percentile of
26 the 1-hour daily maximum SO₂ concentrations) where the SO₂ effect estimate remained positive
27 and statistically significant in multipollutant models with PM (NYDOH (2006), Ito et al., (2007),
28 and Schwartz et al., (1995)). The Administrator judged these three studies were of particular
29 relevance because they supported both the conclusion that SO₂ effects were generally
30 independent of PM and that these associations occurred in cities with 1-hour daily maximum,
31 99th percentile concentrations in the range of 78–150 ppb (74 FR at 35547).

32 Weighing all of the evidence presented above, the Administrator concluded that the
33 epidemiologic studies provided strong support for setting a standard that limited the 99th

²⁷ The REA considered 5-minute air quality data reported from the existing network of ambient monitors. However, since the number and geographic scope of monitors reporting 5-minute SO₂ concentrations was very limited, the REA used statistically estimated 5-minute concentrations derived from measured 1-hour SO₂ concentrations in the 40 county air quality analysis (see below, section 5.1).

1 percentile of the distribution of 1-hour daily maximum SO₂ concentrations to 75 ppb. This
2 judgment took into account the strong determinations in the ISA, based on a much broader body
3 of evidence, that there is a causal relationship between exposure to SO₂ and the types of
4 respiratory morbidity effects reported in these studies (74 FR at 35548). This judgement also
5 considered that a standard level of 75 ppb was consistent with the range of levels recommended
6 by CASAC (75 FR at 35548). Finally, the Administrator acknowledged that there were some
7 epidemiologic studies suggesting effects due to SO₂ at concentrations as low as 50 ppb, but did
8 not find that evidence strong enough to warrant a standard at that level or below (74 FR at
9 35548).

10 **Revoking the Then-Existing 24-hour and Annual Standards**

11 In addition to setting a new 1-hour standard at 75 ppb, the then-current 24-hour and
12 annual standards were revoked in the last review based largely on the recognition that a 1-hour
13 standard set at 75 ppb would have the effect of generally maintaining 24-hour and annual SO₂
14 concentrations well below the levels of those standards (75 FR at 35550). In addition, the annual
15 standard was also revoked because of the lack of evidence supporting a relationship between
16 long-term SO₂ exposures and adverse health effects. That is, the ISA judged the health evidence
17 linking long-term SO₂ exposure to adverse health effects to be “inadequate” to infer the presence
18 or absence of a causal relationship (75 FR at 35550 and U.S EPA 2008, section 5.5).

19 **3.1.3 Areas of Uncertainty**

20 While the available scientific information informing the review completed in 2010 was
21 stronger and more consistent than in previous reviews and provided a strong basis for decisions
22 made in that review, the Agency recognized that important uncertainties and limitations remain
23 in our understanding of several policy-relevant issues. These uncertainties were generally
24 related to: (1) statistical relationships between 5-minute concentrations and longer averaging
25 times (e.g., 1-hour, 3-hour, 24-hour), including the extent to which these longer averaging times
26 can limit 5-minute concentrations of concern (i.e., 5-minute benchmarks) identified from
27 controlled human exposure studies; (2) understanding the role of SO₂ within the complex
28 ambient mixture of co-occurring pollutants (e.g., PM_{2.5}, ozone, NO₂); (3) understanding the
29 range of ambient concentrations in which we have confidence that the health effects observed in
30 epidemiologic studies are attributable to SO₂; (4) the extent to which monitored ambient SO₂
31 concentrations used in epidemiologic studies reflect exposures in study populations and; (5)
32 characterization of SO₂ exposures and risk including alternative approaches for estimating risks
33 associated with air quality simulated to just meet current or alternative standards.

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3.2 GENERAL APPROACH FOR THE CURRENT REVIEW

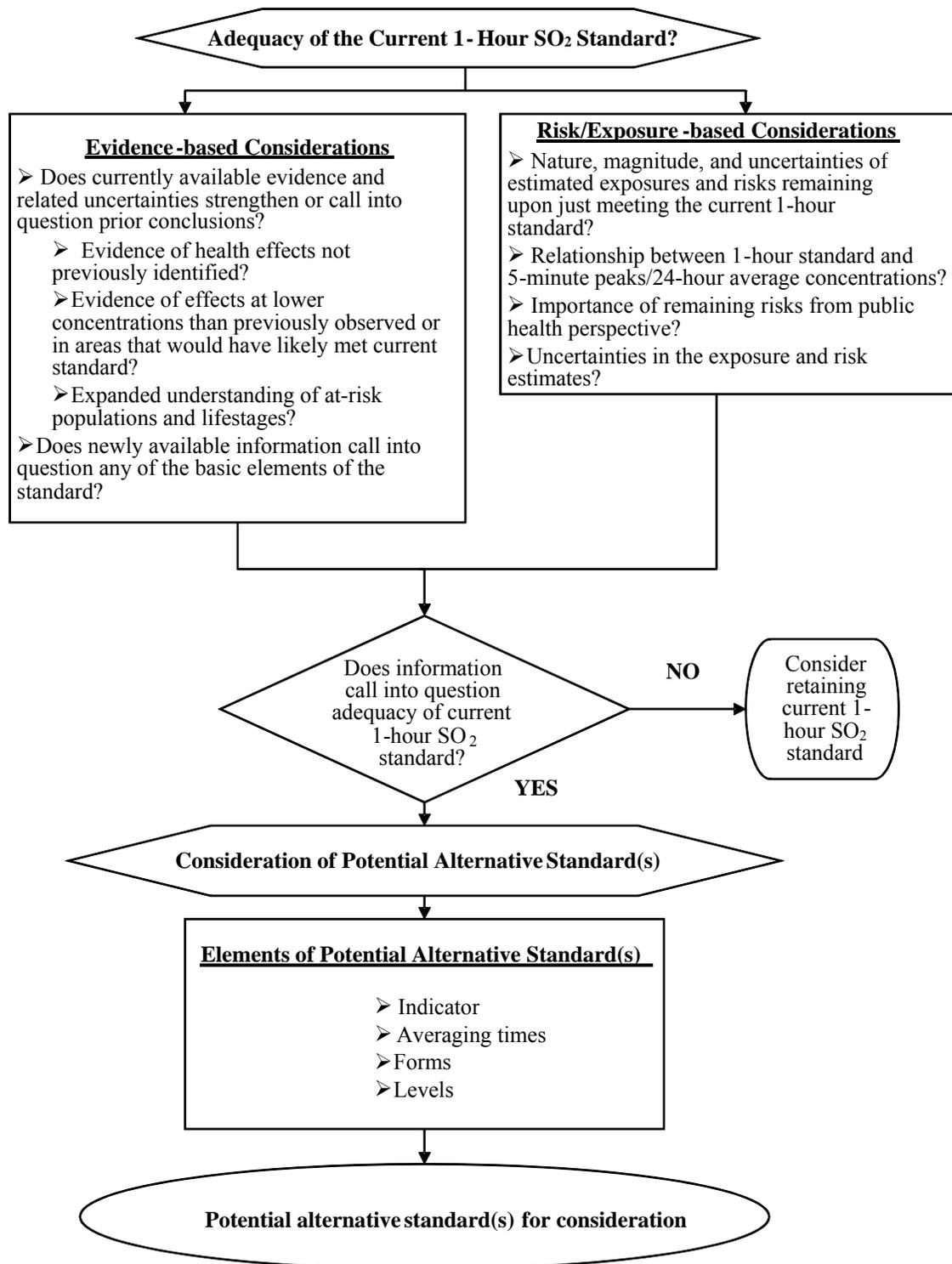
The approach for this review builds on the substantial body of work done during the course of the last review, and will take into account the more recent scientific information and air quality data now available to inform our understanding of the key policy-relevant issues. The approach described below is most fundamentally based on using the EPA's assessment of the current scientific evidence and associated quantitative analyses to inform the Administrator's judgments regarding primary standards for sulfur oxides that are requisite to protect public health with an adequate margin of safety. This approach will involve translating scientific and technical information into the basis for addressing a series of key policy-relevant questions using both evidence- and exposure/risk-based considerations.²⁸

Figure 3-1 summarizes the general approach, including consideration of the policy-relevant questions which will frame the current review. The ISA, REA (if warranted), and PA developed in this new review will provide the basis for addressing the key policy-relevant questions and will inform the Administrator's judgment as to the adequacy of the current primary SO₂ standard and decisions as to whether to retain or revise this standard. This approach recognizes that the available health effects evidence generally reflects a continuum, consisting of ambient concentrations at which scientists generally agree that health effects are likely to occur, through lower concentrations at which the likelihood and magnitude of the response become increasingly uncertain. Furthermore, this approach is consistent with the requirements of the NAAQS provisions of the CAA and with how the EPA and the courts have historically interpreted the CAA. As discussed in section 1.1 above, these provisions require the Administrator to establish primary standards that, in the Administrator's judgment, are requisite to protect public health with an adequate margin of safety. In so doing, the Administrator seeks to establish standards that are neither more nor less stringent than necessary for this purpose. The CAA does not require that primary standards be set at a zero-risk level, but rather at a level that avoids unacceptable risks to public health. The four basic elements of the NAAQS (i.e., indicator, averaging time, form, and level) will be considered collectively in evaluating the health protection afforded by the current standard or any alternative standards considered.

We note that the final decision on the adequacy of the current standard and, if appropriate, potential alternative standards, is largely a public health policy judgment to be made by the Administrator. The Administrator's final decision must draw upon scientific information and analyses about health effects, population exposure and risks, as well as judgments about how to consider the range and magnitude of uncertainties that are inherent in the scientific evidence

²⁸ Evidence-based considerations include those related to the health effects evidence assessed and characterized in the ISA. Exposure/risk-based considerations draw from the results of the quantitative analyses.

1 and analyses. As in the previous review as well as other recent NAAQS reviews, the EPA will
2 consider the implications of placing more or less weight or emphasis on different aspects of the
3 scientific evidence and exposure/risk-based information to inform the public health policy
4 judgments that the Administrator will make in reaching final decisions on whether to retain or
5 revise the current standard in this review.
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Figure 3-1 Overview of General Approach for Review of Primary SO₂ Standard

1 The initial overarching question in reviewing the adequacy of the current primary SO₂
2 NAAQS is whether the available body of scientific evidence, assessed in the ISA and used as a
3 basis for developing or interpreting risk/exposure analyses, supports or calls into question the
4 scientific conclusions reached in the last review regarding health effects related to exposures to
5 sulfur oxides. The evaluation of the available scientific evidence and risk/exposure information
6 with regard to adequacy of the current standard will focus on key policy-relevant issues by
7 addressing a series of questions including the following:

- 8 • To what extent has new information altered the scientific support for the occurrence of
9 health effects as a result of short- and/or long-term exposure to sulfur oxides in the
10 ambient air?
 - 11 ○ What evidence is available from recent studies focused on specific chemical
12 components within the broader group of sulfur oxides (e.g., SO₂, SO₃) to inform
13 our understanding of the nature of exposures that are linked to various health
14 outcomes?
 - 15 ○ To what extent is key scientific evidence becoming available to improve our
16 understanding of the health effects associated with various time periods of
17 exposures, including short-term (e.g., 5-minute, 1-hour, 24-hour) and chronic
18 exposures (e.g., months to years)?
 - 19 ○ At what pollutant concentrations do these health effects occur? Is there evidence
20 of effects at exposure concentrations lower than have been previously observed or
21 in areas that would likely meet the current SO₂ primary standard?
 - 22 ○ To what extent are health effects associated with exposures to sulfur oxides,
23 including SO₂, as opposed to one or more co-occurring pollutants (e.g., PM_{2.5},
24 ozone, NO₂)?
 - 25 ○ What are the important uncertainties and limitations associated with the scientific
26 evidence?
- 27 • Has new information altered our understanding of human lifestages and populations that
28 are particularly at increased risk for experiencing health effects associated with exposure
29 to sulfur oxides?
 - 30 ○ Is there new information to shed light on the nature of the exposure-response
31 relationship in different at-risk lifestages and/or populations?
 - 32 ○ Is there new or emerging evidence on health effects beyond respiratory effects in
33 asthmatics, children, and the elderly that suggest additional at-risk populations
34 and lifestages should be given increased focus in this review?
- 35 • What are the air quality relationships between short-term and longer-term exposures
36 to SO₂?
 - 37 ○ As noted in section 1.3, as part of the final rulemaking the EPA for the first time
38 required state reporting of either the highest 5-minute concentration for each hour
39 of the day, or all twelve 5-minute concentrations for each hour of the day. To

1 what extent can this 5-minute monitoring data collected since the last review be
2 used to further characterize the relationship between 5-minute peaks and longer
3 term (e.g., 1-hour, 3-hour, 24-hour) average concentrations?

4 ○ What are the important uncertainties associated with using a 1-hour NAAQS to
5 protect against 5-minute peak concentrations of concern?

6 • To what extent does risk or exposure information suggest that exposures of concern (i.e.,
7 exposures above benchmark levels) are likely to occur with recent ambient SO₂
8 concentrations or with concentrations that just meet the current SO₂ standard?

9 ○ Are the estimated risks/exposures considered in this review of sufficient
10 magnitude such that the health effects might reasonably be judged to be important
11 from a public health perspective?

12 ○ What are the important uncertainties associated with any risk/exposure estimates?

13 • To what extent have important uncertainties identified in the last review been reduced
14 and/or have new uncertainties emerged?

15 • To what extent does newly available information reinforce or call into question any of the
16 basic elements of the current primary SO₂ standard?

17 If the evidence suggests that revision of the current standard might be appropriate, the
18 EPA will evaluate how the standard might be revised. Specifically, we will evaluate how the
19 scientific information and assessments inform decisions regarding the basic elements of the
20 primary SO₂ NAAQS: indicator, averaging time, form and level. These elements will be
21 considered collectively in evaluating the health protection afforded by the current or any
22 alternative standard(s) considered. Specific policy-relevant questions related to these standard
23 elements include:

24 • To what extent does any new information provide support for the continued use of SO₂ as
25 the *indicator* for sulfur oxides? Is there evidence to support using an *indicator* in
26 addition to, or in place of SO₂?

27 • To what extent does the health effects evidence evaluated in the ISA continue to provide
28 support for the existing 1-hour *averaging time*? Does the currently available information
29 provide support for considering any different *averaging times*?

30 • To what extent do air quality analyses conducted since the last review suggest a standard
31 with an *averaging time* of 1-hour or longer can protect against 5-minute and/or 24-hour
32 concentrations of concern? Do these air quality analyses provide support for considering
33 any different *averaging times*?

34 • To what extent do the ISA, air quality analyses, and other information provide support for
35 consideration of alternative standard *forms*?

- 1 • What range of alternative standard *levels* should be considered based on the scientific
2 evidence evaluated in the ISA, air quality analyses and, if available, in the REA²⁹ ?
- 3 • What are the important uncertainties and limitations in the available evidence and
4 assessments and how might those uncertainties and limitations be taken into
5 consideration in identifying alternative standard *indicators, averaging times, forms,*
6 *and/or levels?*

²⁹ As outlined in Table 2-1 and discussed in Chapter 5 below, the REA Planning Document will consider the extent to which newly available scientific evidence and tools/methodologies warrant the conduct of new quantitative risk and exposure assessments. To the extent completely new assessments are not developed for this review, assessments from the last review may be interpreted in light of the newly available information in addressing the key policy questions for the review.

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4. SCIENCE ASSESSMENT

The ISA comprises the science assessment phase of the SO₂ NAAQS review. As described in section 1.4 above, this assessment focuses on updating the air quality criteria associated with health evidence to inform the review of the primary SO₂ standard only.³⁰

4.1 SCOPE OF THE ISA

The ISA will critically evaluate and integrate the scientific information on exposure and health effects associated with SO_x in ambient air in the discipline areas of atmospheric science, human exposure, dosimetry, epidemiology, controlled human exposure, and toxicology. The purpose of the discussions within the ISA is not to provide a detailed literature review but to draw upon the existing body of evidence to synthesize the current state of knowledge on the most relevant issues pertinent to the review of the NAAQS for SO₂, to identify changes in the scientific evidence base since the previous review, and to describe remaining or newly identified uncertainties. The ISA discussions will be designed to focus on the key policy-relevant questions described in Section 3.4.

The current ISA will focus on literature published since the 2008 SO_x ISA and integrate this newer evidence with evidence considered in the last review. Key findings, conclusions, and uncertainties from the 2008 ISA for SO_x will be briefly summarized at the beginning of the ISA and individual sections. The results of recent studies will be integrated with previous findings. In evaluation of controlled human exposure and animal toxicological studies, emphasis will be placed on studies that examine health effects relevant to humans and on SO_x concentrations that represent the range of human exposures across various ambient microenvironments. However, in recognition of the fact that controlled human exposure and animal toxicological studies do not necessarily reflect effects in the most sensitive populations, studies at higher exposure concentrations will be included when they provide information relevant to previously unreported effects, evidence of the potential biological mechanism for an observed effect, or information on exposure-response relationships.

4.2 ORGANIZATION OF THE ISA

The organization of the ISA for health criteria of SO_x will be consistent with that used in the recent assessments for other criteria pollutants, e.g., the ISA for Ozone and Related

³⁰Note 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 NO₂ and SO₂.

1 Photochemical Oxidants (U.S. EPA, 2013b). The ISA will begin with a discussion of major legal
2 and historical aspects of prior review documents as well as procedures for the assessment of
3 scientific information. An integrative synthesis chapter will summarize the key information for
4 each topic area, the causal determinations for relationships between exposure to SO_x and health
5 effects, information describing the extent to which health effects can be attributable specifically
6 to SO_x, and other uncertainties related to the interpretation of scientific information. The
7 integrative synthesis chapter also will present a discussion of policy-relevant issues such as the
8 exposure averaging times and lags associated with health effects, the concentration-response
9 relationships including whether or not the evidence supports identification of a discernible
10 threshold below which effects are not likely to occur, and the public health significance of health
11 effects associated with exposure to SO_x. Subsequent chapters are organized by subject area (see
12 draft outline of the ISA in Appendix A) and contain the detailed evaluation of results of recent
13 studies integrated with previous findings (see section 4.4 for specific issues to be addressed).
14 Sections for each major health effect category (e.g., respiratory effects) conclude with a causal
15 determination about the relationship with relevant exposures to SO_x. The ISA will conclude
16 with a chapter that examines exposure and health outcome data to draw conclusions about
17 potential at-risk lifestages and populations.

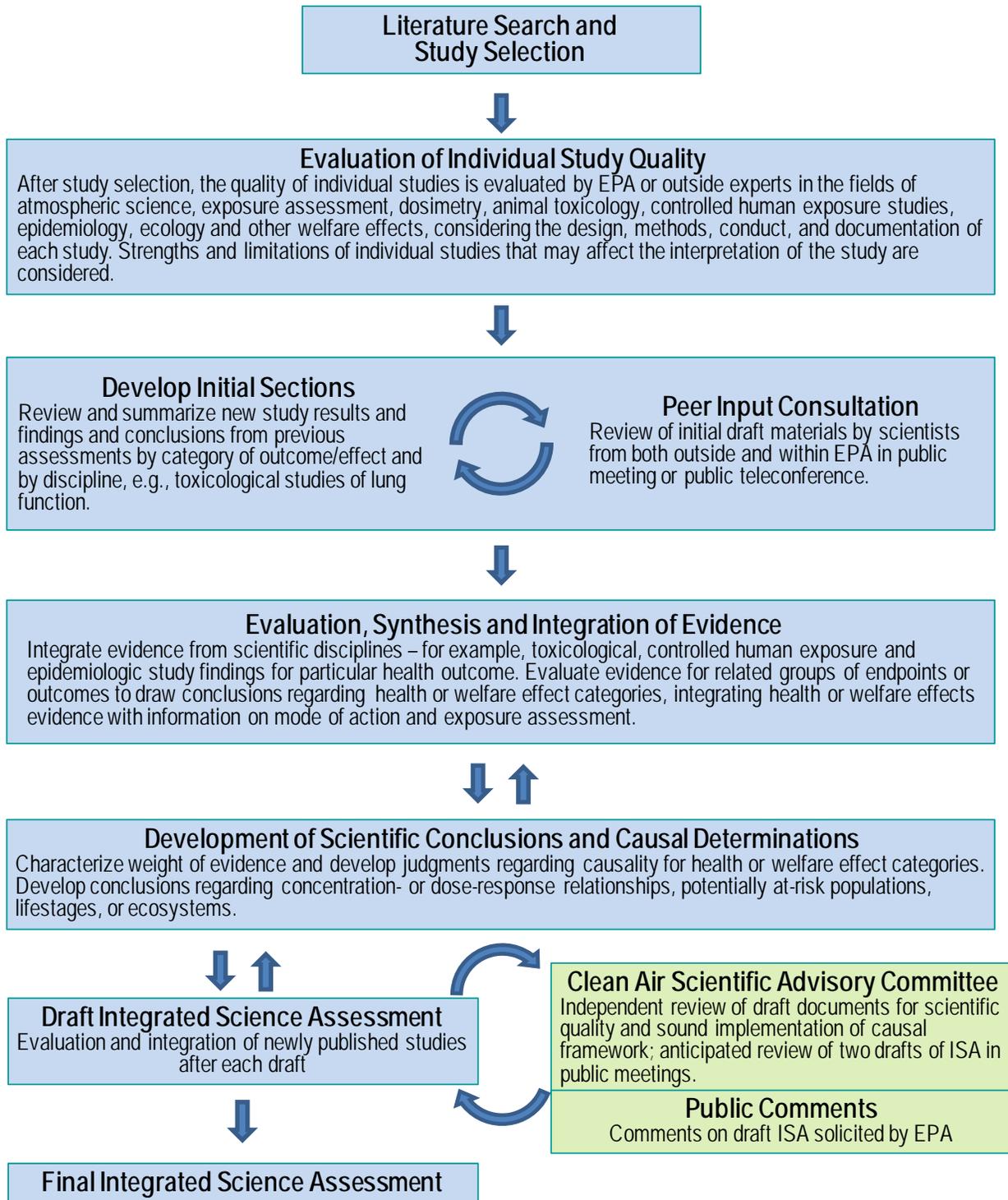
18 The ISA may be supplemented with additional materials if required to support
19 information contained within the ISA. These supplementary materials may include more
20 detailed and comprehensive coverage of relevant publications and may accompany the ISA or be
21 available in electronic form as output from the Health and Environmental Research Online
22 (HERO) database developed by EPA (<http://hero.epa.gov/>). Supplementary information
23 available in the HERO database will be presented as electronic links in the ISA.

24 **4.3 ASSESSMENT APPROACH**

25 **4.3.1 Introduction**

26 The NCEA-RTP is responsible for preparing the ISA for SO_x health criteria. In each
27 NAAQS review, development of the science assessment begins with a “Call for Information”
28 published in the *Federal Register*. This notice announces EPA’s initiation of activities in the
29 preparation of the ISA for the specific NAAQS review and invites the public to assist through the
30 submission of research studies in the identified subject areas. This and subsequent key
31 components of the process currently followed for the development of an ISA (i.e., the
32 development process) are presented in Figure 3.1 and are described in greater detail in the
33 Preamble to the ISA for Lead (U.S. EPA, 2013a). How the ISA fits into the larger NAAQS
34 review process is briefly described in Section 1.2, the Overview of the Review Process.

35



2 **Figure 4.1. General Process for Development of Integrated Science Assessments (ISAs)**
 3 (Modified from Figure III of the Preamble to the ISA for Lead, U.S. EPA, 2013a)

4 Important aspects of the development of the ISA are described in the sections below,
 5 including the approach for searching the literature, identifying relevant publications, evaluating

1 individual study quality, synthesizing and integrating the evidence, and developing scientific
2 conclusions and causality determinations. These responsibilities are undertaken by expert
3 authors of the ISA chapters which include EPA staff with extensive knowledge in their
4 respective fields and extramural scientists solicited by EPA for their expertise in specific fields.
5 This section of the IRP also presents specific policy-relevant questions developed from input
6 received at the SO_x kickoff workshop. These questions are intended to guide the development of
7 the ISA. The process for scientific and public review of drafts of the ISA is described in Section
8 4.3.

9 **4.3.2 Literature Search and Selection of Relevant Studies**

10 The NCEA-RTP uses a structured approach to identify relevant studies for consideration
11 and inclusion in the ISA. A *Federal Register* notice is published to announce the initiation of a
12 review and to request information, including relevant literature, from the public. The EPA
13 maintains an ongoing, multi-tiered literature search process that includes extensive manual and
14 computer-aided citation mining of databases on specific topics in a variety of disciplines using as
15 keywords terms such as SO_x, SO₂, sulfur oxide(s), or sulfur dioxide. The search strategies are
16 designed a priori and iteratively modified to optimize identification of pertinent publications. In
17 addition, papers are identified for inclusion in several other ways: specialized searches on
18 specific topics; relational searches that identify recent publications that have cited references
19 from previous assessments; identification of relevant literature by external scientific experts;
20 recommendations from the public and CASAC during the call for information and external
21 review process; and review of citations in previous assessments. The studies identified will
22 include research published or accepted for publication from January 2008, which slightly
23 precedes the publication end date for studies reviewed in the 2008 SO_x ISA, through
24 approximately two months before the release of the second external review draft of the ISA
25 (target of June 2015, see Table 2-1).

26 References identified through this multipronged search strategy are reviewed for
27 relevance. Some publications are excluded based on screening of the title. Publications
28 considered for inclusion in the ISA after reading the title are listed in the Health and
29 Environmental Research Online (HERO) database (<http://hero.epa.gov>). Studies and reports that
30 have undergone scientific peer review and have been published or accepted for publication are
31 considered for inclusion in the ISA.

32 From the group of considered references, references are selected for inclusion in the ISA
33 based on review of the abstract and full text. The references cited in the ISA include a hyperlink
34 to the HERO database. The selection process is based on the extent to which the study is
35 potentially informative and policy-relevant. Potentially policy-relevant and informative studies
36 include those that provide a basis for or describe the relationship between the criteria pollutant

1 and effects, in particular, those studies that offer innovation in method or design and studies that
2 reduce uncertainty on critical issues. Uncertainty can be addressed, for example, by analyses of
3 potential confounding or effect modification by copollutants or other factors, analyses of
4 concentration-response or dose-response relationships, or analyses related to time between
5 exposure and response. The ISA will generally emphasize studies published since the 2008 SO_x
6 ISA; however, evidence from previous studies will be included to integrate with results from
7 recent studies and, in some cases, characterize the key policy-relevant information in a particular
8 subject area. Analyses conducted by the EPA using publicly available data, for example, air
9 quality and emissions data, also are considered for inclusion in the ISA. The combination of
10 approaches described above is intended to produce the comprehensive collection of pertinent
11 studies needed to address the key scientific issues that form the basis of the ISA.

12 **4.3.3 Evaluation of Individual Study Quality**

13 After selecting studies for inclusion, individual study quality is evaluated by considering
14 the design, methods, conduct, and documentation of each study, but not whether the results are
15 positive, negative, or null. This uniform approach aims to consider the strengths, limitations, and
16 possible roles of chance, confounding, and other biases that may affect the interpretation of the
17 results from individual studies. In assessing the scientific quality of studies, the following
18 parameters are considered:

- 19 • How clearly were the study design, study groups, methods, data, and results presented to
20 allow for study evaluation?
- 21 • To what extent are the air quality data, exposure, or dose metrics of adequate quality to
22 serve as credible exposure indicators?
- 23 • Were the study populations, subjects, or animal models adequately selected, and are they
24 sufficiently well defined to allow for meaningful comparisons between study or exposure
25 groups?
- 26 • Are the statistical analyses appropriate, properly performed, and properly interpreted?
- 27 • Are likely covariates (i.e., potential confounding factors, modifying factors) adequately
28 controlled for or taken into account in the study design or statistical analyses?
- 29 • Are the health endpoint measurements meaningful, valid, and reliable?

30 Additional considerations specific to particular scientific disciplines are discussed below.

31 **Atmospheric Science and Exposure Assessment**

32 Atmospheric science and exposure assessment studies focus on measurement of, behavior
33 of, and exposure to ambient air pollution using quality-assured field, experimental, and/or
34 modeling techniques. The most informative measurement-based studies will include detailed
35 descriptive statistics for high-quality measurements taken at varying spatial and temporal scales.
36 These studies will also include a clear and comprehensive description of measurement

1 techniques and quality control procedures used. Quality control metrics (e.g., method detection
2 limits) and quantitative relationships between and within pollutant measurements (e.g.,
3 regression model coefficients, intercepts, and fit statistics) should be provided when appropriate.
4 Measurements including contrasting conditions for various time periods (e.g., weekday/weekend,
5 season), populations, regions, and categories (e.g., urban/rural, proximity to various source
6 sectors) are particularly useful. The most informative modeling-based studies will incorporate
7 appropriate chemistry, transport, dispersion, and/or exposure modeling techniques with a clear
8 and comprehensive description of model science, evaluation procedures, and metrics.

9 Exposure measurement error, which refers to the uncertainty associated with the exposure
10 metrics used to represent exposure of an individual or population, can be an important
11 contributor to uncertainty in air pollution epidemiologic study results. Exposure measurement
12 error can influence observed epidemiologic associations between ambient pollutant
13 concentrations and health outcomes by biasing effect estimates toward or away from the null and
14 widening confidence intervals around those estimates (Zeger et al., 2000). Factors that could
15 influence exposure estimates include, but are not limited to, nonambient sources of exposure,
16 topography of the natural and built environment, meteorology, air quality measurement
17 instrument or model uncertainties, time-activity patterns, and the infiltration into indoor
18 environments. Additional information present in high-quality exposure studies includes location
19 and activity information from diaries, questionnaires, global positioning system data, or other
20 means, as well as information on commuting patterns. In general, atmospheric science and
21 exposure studies focusing on the variety of locations pertinent to the range of exposures in the
22 U.S. will have maximum value in informing review of the NAAQS.

23 **Epidemiology**

24 In evaluating quality of epidemiologic studies, EPA additionally considers whether a
25 given study: (1) presents quantitative information on associations of health effects with short- or
26 long-term exposures that represent ambient concentrations of SO_x across various
27 microenvironments; (2) examines health effects of SO_x; (3) assesses SO_x as a component of a
28 complex mixture of air pollutants by considering concentrations of copollutants, correlations of
29 SO_x with these copollutants, potential copollutant interactions (e.g., synergistic effects of SO_x
30 with other pollutants), potential copollutant confounding (e.g., bias of associations observed
31 between SO_x and health endpoints by the effects of copollutants), and other methods to assess
32 the independent effect of SO_x; (4) evaluates health endpoints not previously extensively
33 researched; (5) evaluates lifestyles and populations that potentially are at increased risk of health
34 effects related to SO_x; (6) examines other potential confounding factors or effect modifiers (e.g.,
35 socioeconomic status); and (7) examines important methodological issues (e.g., lag or time
36 period between exposure and effects, model specifications, thresholds, mortality displacement)

1 related to the health effects of exposure to SO_x. Among epidemiologic studies characterized as
2 high quality by these parameters, emphasis will be given to multicity studies that employ
3 standard methodological analyses for evaluating effects of SO_x across cities, provide overall
4 estimates for effects by pooling information across cities, and examine consistency of results
5 across cities. To address specific issues relevant to standard setting in the U.S., such as regional
6 heterogeneity in effects, emphasis will be placed on studies that involve exposures that are
7 relevant to current U.S. populations (e.g., studies conducted in the U.S. or Canada).

8 **Controlled Human Exposure and Animal Toxicology**

9 Controlled human exposure and animal toxicological studies experimentally evaluate the
10 health effects of administered exposures in human volunteers and animal models under highly
11 controlled laboratory conditions. Controlled human exposure studies are also referred to as
12 human clinical studies and, as noted above, provided the definitive evidence for a causal
13 relationship between short-term exposure to SO₂ and respiratory morbidity in the previous
14 review. These experiments allow investigators to expose subjects to known concentrations of
15 SO_x under carefully regulated environmental conditions and activity levels. In addition to the
16 general quality considerations discussed previously, evaluation of controlled human exposure
17 and animal toxicological studies includes assessing the design and methodology of each study
18 with focus on (1) characterization of the intake dose, dosing regimen (e.g., duration, activity
19 level), and exposure route; (2) characterization of the pollutant(s); (3) sample size and statistical
20 power to detect differences; and (4) control of other variables that could influence the occurrence
21 of effects. The evaluation of study design generally includes consideration of factors that
22 minimize bias in results such as randomization, blinding and allocation concealment of study
23 subjects, investigators, and research staff, and unexplained loss of animals or
24 withdrawal/exclusion of subjects. Additionally, studies must include appropriate control groups
25 and exposures to allow for accurate interpretation of results relative to exposure. Emphasis is
26 placed on studies that address concentration-dependent responses or time-course of responses
27 and studies that investigate potentially at-risk lifestages and populations (e.g., with pre-existing
28 disease), recognizing that controlled human exposure studies typically examine effects in groups
29 of relatively healthy individuals, often adults, who do not represent the full range of
30 susceptibilities in the general population. In addition, consideration will be given to studies that
31 investigate exposure to SO_x separately and in combination with other pollutants such as ozone
32 and particulate matter.

33 Controlled human exposure or animal toxicological studies that approximate expected
34 human exposures in terms of concentration, duration, and route of exposure are of particular
35 interest. Relevant pollutant exposures are considered to be those generally within two orders of
36 magnitude of ambient concentrations measured across various microenvironments. Studies using

1 higher concentration exposures or doses will be considered to the extent that they provide
2 information relevant to understanding mode of action or mechanisms, interspecies variation, or
3 at-risk human lifestages and populations. In vitro studies may be included if they provide
4 mechanistic insight or support results demonstrated in vivo.

5 **4.3.4 Integration of Evidence and Determination of Causality**

6 EPA has developed a consistent and transparent basis for integration of scientific evidence
7 and evaluation of the causal nature of air pollution-related health or welfare effects for use in
8 developing ISAs, as described in the online Preamble to the ISA for Lead (U.S. EPA, 2013a).
9 Evidence from across scientific disciplines for related health effects is evaluated, synthesized,
10 and integrated to develop conclusions and causality determinations. This includes consideration
11 of strengths and weaknesses in the overall collection of studies across disciplines. Confidence in
12 the body of evidence is based on evaluation of study design and quality. The relative importance
13 of different types of evidence to the conclusions varies by pollutant or assessment, as does the
14 availability of different types of evidence for causality determination. Consideration of human
15 health effects is informed by controlled human exposure, epidemiologic, and toxicological
16 studies. Other evidence including mechanistic evidence, toxicokinetics, and exposure assessment
17 may be highlighted if it is relevant to the evaluation of health effects and if it is of sufficient
18 importance to affect the overall evaluation. Scientists will also evaluate uncertainty in the
19 scientific evidence, considering issues such as generalizing results from a small number of
20 controlled human exposure subjects to the broader population, quantitative extrapolations of
21 observed pollutant-induced pathophysiological alterations from laboratory animals to humans,
22 confounding by co-exposure to other ambient pollutants or meteorological factors, the potential
23 for effects due to exposure to air pollution mixtures, and the influence of exposure measurement
24 error on epidemiologic study findings.

25 The ISA will evaluate the evidence for causal relationships between observed health
26 outcomes and SO_x exposures using a five-level hierarchy that classifies the weight of evidence
27 for causation. Determination of causality involves the evaluation and integration of evidence
28 across disciplines for major outcome categories (e.g., respiratory effects) or groups of related
29 endpoints. Key considerations in drawing conclusions about causality include consistency of
30 findings for an endpoint across studies, biological plausibility, and coherence of the evidence
31 across disciplines and across related endpoints, including key events that inform modes of action
32 (see Table I in Preamble to the ISA for Lead, U.S. EPA, 2013a). In discussing the causal
33 determination, EPA characterizes the evidence on which the judgment is based, including

1 strength of evidence for individual endpoints within the outcome category or group of related
2 endpoints. The ISA will place emphasis on studies conducted with SO_x exposure concentrations
3 representative of those across various ambient microenvironments. However, studies that provide
4 evidence for biological plausibility and modes of action, which are conducted at higher exposure
5 concentrations than those typically associated with health effects in humans, may be included in
6 the ISA. In addition, EPA evaluates evidence relevant to understand the quantitative
7 relationships between pollutant exposures and health effects. This includes evaluating the
8 concentration-response or dose-response relationships and, to the extent possible, drawing
9 conclusions on the levels at which effects are observed.

10 **4.3.5 Quality Management**

11 NCEA participates in the Agency-wide Quality Management System, which requires the
12 development of a Quality Management Plan (QMP). Implementation of the ORD-wide and
13 NCEA QMP ensures that all data generated or used by NCEA scientists “have a degree of
14 confidence in the quality of the data; and, are of the type and quality appropriate for their
15 intended use” and that all information disseminated by NCEA adheres to a high standard for
16 quality including objectivity, utility, and integrity. Quality assurance (QA) measures detailed in
17 the QMP are being employed for the current SO_x review, including the development of the ISA
18 for health criteria of SO_x. The NCEA QA staff are responsible for the review and approval of
19 quality-related documentation. NCEA scientists are responsible for the evaluation (and
20 documentation) of all inputs to the ISA, including primary (new) and secondary (existing) data,
21 to ensure their quality is appropriate for their intended purpose. NCEA adheres to the use of
22 Data Quality Objectives, which clarify project objectives, define the appropriate type of data
23 used in the project, and specify tolerable levels of confidence in the data and tolerable levels of
24 potential decision errors that will be used as the basis for establishing the quality and quantity of
25 data needed to identify the most appropriate inputs to the science assessment. The approaches
26 utilized to search the literature and criteria for study selection and evaluation were detailed in the
27 two preceding subsections. Generally, NCEA scientists rely on scientific information found in
28 peer-reviewed journal articles, books, and government reports. Where information is integrated,
29 re-analyzed, modeled, or reduced from multiple sources to create new figures, tables, or
30 summation, the data generated are considered to be new and are documented and subjected to
31 rigorous quality assurance and quality control measures to ensure their accuracy, validity, and
32 reproducibility.

1 **4.4 SPECIFIC ISSUES TO BE ADDRESSED IN THE ISA**

2 The organization of the ISA for SO_x health criteria will be consistent with that used in
3 the recent assessments for other criteria pollutants (e.g., [ISA for O₃, U.S. EPA, 2013b](#)).
4 Development of the ISA will be guided by policy-relevant questions that frame the entire review
5 of the primary SO₂ NAAQS. These policy-relevant questions are related to two overarching
6 issues. The first issue is whether new evidence reinforces or calls into question the evidence
7 presented and evaluated in the last NAAQS review with respect to factors such as the
8 concentrations of SO_x exposure associated with health effects and plausibility of health effects
9 caused by SO_x exposure. The second issue is whether uncertainties from the last review have
10 been reduced and/or whether new uncertainties have emerged. Specific questions that will be
11 addressed in the ISA are listed subsequently by topic area. In the ISA, these topic areas will be
12 discussed in separate chapters or sections. The beginning of the ISA will include an integrative
13 synthesis chapter that summarizes the key information for each topic area and the causal
14 determinations. The integrative synthesis chapter also presents a discussion of policy-relevant
15 issues such as the exposure metrics, averaging times, and lags associated with health effects, the
16 concentration-response relationship including threshold for effects, and public health
17 significance of health effects associated with exposure to SO_x (see Appendix).

18
19 A. Air Quality and Atmospheric Chemistry: The ISA will present and evaluate data related
20 to ambient concentrations of SO_x; sources leading to the presence of SO_x in the
21 atmosphere; and chemical reactions that determine the formation, degradation, and
22 lifetime of SO_x in the atmosphere. The 2008 SO_x ISA concluded that most SO₂ is
23 emitted from elevated point sources such as the stacks of power plants and industrial
24 facilities, many of which are located in the eastern U.S., leading to a strong east-west
25 gradient in SO₂ concentrations. SO₂ is removed from the atmosphere both by deposition
26 and by oxidation to sulfate, resulting in a typical atmospheric lifetime of <1 to 4 days,
27 depending on local conditions. Mean U.S. daily 1-hour max SO₂ concentrations in 2003-
28 05 were approximately 13 ppb, with a 99th percentile value of 95 ppb and a maximum
29 value of approximately 700 ppb. The large differences between 99th percentile and
30 maximum values suggest that the maxima are strongly limited spatially and temporally
31 and are not a major determinant of the mean values. At the time of the 2008 SO_x ISA, the

1 very limited 5-minute SO₂ data available showed that the median hourly maximum 5-
2 minute average ranged from 1-8 ppb, while the 99th percentile value ranged from 21-184
3 ppb, depending on location (U.S. EPA, 2008, section 5.1). In the current ISA, description
4 of the atmospheric chemistry of SO_x will include both gaseous and particulate species in
5 order to provide a complete analysis, although the health effects of particulate SO_x are
6 discussed in the review of the NAAQS for particulate matter (PM). SO₂ is the most
7 important of the gas-phase sulfur oxides for both atmospheric chemistry and health
8 effects and is expected to be the focus of the ISA. SO_x is usually defined to include sulfur
9 trioxide (SO₃) and gas-phase sulfuric acid (H₂SO₄) as well, but neither species is present
10 in the atmosphere in concentrations significant for human exposures. In the current
11 review, specific policy-relevant questions related to air quality and atmospheric
12 chemistry that will be addressed include the following:

- 13 • What are the main and emerging sources of ambient gas-phase SO_x, and how have new
14 fuels, emission standards, and technologies changed the magnitude and composition of
15 SO_x emissions?
- 16 • What progress has been made in improving measurements and reducing interference
17 problems in measuring SO_x, particularly for concentrations near the method detection
18 limit? What limitations still remain?
- 19 • Based on recent air quality and emissions data, what are current emissions and
20 concentrations of SO_x? How have emissions and concentrations of SO_x changed since
21 the 2008 SO_x ISA? To what extent can other techniques, such as satellite data and
22 dispersion modeling, be used to improve the characterization of SO_x concentrations?
- 23 • What spatial and temporal patterns can be seen in SO_x concentrations? In particular,
24 what patterns can be seen near point and other sources of SO_x? What do monitoring,
25 satellite data, and dispersion modeling results indicate regarding spatial patterns on
26 neighborhood, urban, regional, and national scales?
- 27 • What are the relationships among SO_x concentrations measured with different averaging
28 times (e.g., 5-minute, 1-hour, 24-hour)? How well do 1-hour or longer averaging time
29 concentrations represent peak exposures to SO_x?
- 30 • What are the relationships among SO_x concentrations and concentrations of other
31 pollutants, such as sulfate, other components of particulate matter, and gaseous
32 pollutants?
- 33 • What are the capabilities of air quality models for estimating SO_x concentrations,
34 particularly at the upper end of the air quality distribution?
- 35 • Based on air quality and emissions data on SO_x and atmospheric chemistry models, what
36 are likely background concentrations of SO_x in the absence of anthropogenic emissions?

1 B. Human Exposure to Ambient SO_x: The ISA will evaluate the factors that influence
2 human exposure to ambient SO_x and the uncertainties associated with extrapolation from
3 ambient concentrations to personal exposures to SO_x of ambient origin, particularly in
4 the context of interpreting results from epidemiologic studies. As described in the 2008
5 SO_x ISA, many exposure studies were unable to characterize the relationship between
6 personal exposure and ambient SO₂ due to indoor and outdoor concentrations that were
7 below the detection limit of passive personal samplers. However, in studies with personal
8 measurements above detection limits, a reasonably strong association was observed
9 between personal SO₂ exposure and ambient concentrations (U.S. EPA, 2008, section
10 5.3). At the time of the 2008 SO_x ISA, no studies had evaluated the relationship between
11 community average exposure and ambient concentrations, which is more directly relevant
12 to many epidemiologic study designs, although the ISA concluded that intracommunity
13 variations in the personal-ambient relationship would generally tend to widen the
14 confidence interval rather than bias the effect estimate. Uncertainties differ according to
15 the exposure period of interest as most short-term exposure studies (e.g., population-level
16 studies using time-series analyses, field/panel studies) rely on temporal variation in
17 exposure while long-term exposure studies (e.g., longitudinal cohort studies) rely on
18 spatial variability of exposure. In the current review, specific policy-relevant questions
19 related to exposure that will be addressed include the following:

- 20 • What are the relationships between SO_x measured at stationary monitoring sites and
21 personal exposure to SO_x over different time scales? What evidence is available
22 regarding these relationships in environments near point sources, ports, or other sources?
23 What uncertainties remain regarding these exposures of interest?
- 24 • What new information is available regarding microenvironmental SO_x concentrations
25 and personal exposures to SO_x? What are the capabilities of currently available exposure
26 measurement techniques?
- 27 • What new information exists regarding characterization of error in SO_x exposure
28 assessment and how it influences personal-ambient exposure relationships?
- 29 • What information is available regarding differences in SO_x exposure patterns and
30 personal-ambient exposure relationships among various lifestages and populations,
31 particularly at-risk groups?
- 32 • What new information exists regarding SO_x measurements in a multipollutant context?
33 What are the relationships between SO_x exposures and exposures for other pollutants,
34 such as sulfate, other components of particulate matter, and gaseous pollutants?

- 1 • How does uncertainty in exposure estimates inform interpretation of epidemiologic,
2 controlled human exposure, and toxicological studies?
- 3 C. Dosimetry and Modes of Action: The ISA will evaluate literature focusing on dosimetry
4 and modes of action that may underlie the health outcomes associated with exposure to
5 SO_x. These topic areas will be evaluated using both human and animal data. The 2008
6 SO_x ISA concluded that SO₂ is readily absorbed in the nasal passages due to its high
7 water solubility; with increased ventilation rates during exercise, the pattern of SO₂
8 absorption shifts from the upper airways to the tracheobronchial airways in conjunction
9 with a shift from nasal to oronasal breathing (U.S. EPA, 2008, section 5.2). The
10 compound most directly responsible for the health effects may be the inhaled SO₂ and/or
11 its chemical reaction products such as hydrogen ions, bisulfite anions and sulfite anions
12 which are formed when SO₂ contacts the fluids lining the airway. One of the principal
13 effects of inhaled SO₂ is bronchoconstriction, mediated by chemosensitive receptors that
14 trigger nervous system reflexes. Preexisting inflammation may lead to enhanced
15 sensitivity in asthmatics due to enhanced release of mediators, alterations in the
16 autonomic nervous system, and/or sensitization of the chemosensitive receptors. In the
17 current review, specific policy-relevant questions related to dosimetry and modes of
18 action that will be addressed include the following:
- 19 • What SO_x reaction products can be found in the respiratory tract cells, tissues, or fluids
20 that may serve as markers of SO_x exposure and effect?
- 21 • What information is available on the following dosimetric and mechanistic factors:
- 22 ○ The regional pattern of SO_x-induced injury/perturbation in the respiratory
23 tract?
- 24 ○ Inter-individual variability of responses that may enhance the risk of an
25 adverse health effect?
- 26 ○ Homology of responses between animals and humans?
- 27 • What are the potential biological mechanisms underlying responses to SO_x at or near
28 environmentally relevant exposures?
- 29 • What new information is available related to the modes of action for health effects
30 associated with exposure to SO_x?
- 31 • Do interactions between inhaled SO_x and other inhaled pollutants influence the
32 mechanisms underlying the toxic potential of SO_x?

- 1 • What are the effects of host factors such as lifestage, sex, pre-existing disease, genetic
2 background, and physical activity on SO_x uptake, cellular and tissue responses, and their
3 underlying mechanisms? Are there critical windows of exposure (e.g. prenatal) that result
4 in different effects and/or effects at lower exposures?
- 5 • What information is available to discern the relative contributions to internal SO_x
6 compounds of SO_x derived exogenously from ambient exposures and SO_x derived from
7 endogenous biological processes?

8 D. Health Effects: The 2008 SO_x ISA concluded that there is a causal relationship between
9 respiratory morbidity and short-term exposure to SO₂, based on consistent and coherent
10 evidence from controlled human exposure, epidemiologic, and animal toxicological
11 studies. The definitive evidence for the causal relationship came from controlled human
12 exposure studies that reported respiratory symptoms and decreased lung function in
13 exercising asthmatics following 5-10 minute exposures to SO₂; in addition, numerous
14 epidemiologic studies reported associations between short-term SO₂ exposures and
15 respiratory symptoms and hospitalizations (U.S. EPA, 2008, section 5.2). The ISA also
16 concluded that the evidence is suggestive of a causal relationship between short-term
17 exposure to SO₂ and mortality, and that the evidence is inadequate to infer a causal
18 relationship between short-term exposure to SO₂ and cardiovascular effects or between
19 long-term exposure to SO₂ and morbidity and mortality. The current ISA will evaluate the
20 literature related to respiratory, cardiovascular, reproductive and developmental health
21 effects, mortality, and cancer associated with SO_x exposure. Other health effects may also
22 be evaluated, such as those related to the central nervous system. Health effects that occur
23 following both short- and long-term exposures will be evaluated as examined in
24 epidemiologic, controlled human exposure, and animal toxicological studies, and causality
25 determinations will be developed for each type of health effect. Efforts will be directed at
26 identifying the lower concentrations at which effects are observed, including effects in
27 populations and lifestages potentially at increased risk of SO_x -induced health effects, and
28 assessing the role of SO_x within the broader mixture of ambient pollutants. The discussion
29 of health effects also will be integrated with relevant information on dosimetry and modes
30 of action. In the current review, specific policy-relevant questions related to health effects
31 that will be addressed include the following:

- 32 • What do controlled human exposure, animal toxicological, and epidemiologic studies
33 indicate regarding the relationship between short-term (i.e., minutes to one month)

1 exposures to SO_x and health effects of concern, including the nature and time course, in
2 healthy individuals and in those with pre-existing disease states (e.g., people with asthma
3 or cardiovascular disease) or other factors (e.g., lifestage, genetic variants, nutritional
4 deficiencies) that potentially modify the risk of SO_x-induced health effects? What
5 information is available that reduces uncertainties identified in the previous ISA, such as
6 exposure measurement error and the potential for copollutant confounding?

- 7 • How do results of recent studies expand current understanding of the relationships
8 between long-term (i.e. more than one month to years) exposure to SO_x and chronic
9 respiratory effects manifested as permanent lung tissue damage, a reduction in baseline
10 lung function, or a reduction in lung function growth? To what extent does long-term
11 SO_x exposure promote exacerbation and development of asthma or other chronic lung
12 diseases, cardiovascular diseases, and other conditions? Are there certain lifestages that
13 are especially vulnerable to the development of these chronic conditions? What is the
14 relationship between SO_x exposure and all-cause mortality and cause-specific mortality?
- 15 • To what extent does the scientific evidence support the occurrence of health effects from
16 long-term SO_x exposure at ambient concentrations that are lower than those previously
17 observed? If so, what uncertainties are related to these associations and are the health
18 effects in question important from a public health perspective?
- 19 • To what extent does short-term or long-term exposure to SO_x contribute to health effects
20 beyond the respiratory and cardiovascular systems (e.g., reproductive, developmental,
21 cancer)?
- 22 • What is the extent of coherence of findings for small changes in lung function, airway
23 hyperresponsiveness, heart rate variability, and vasomotor function and changes in health
24 effects such as hospital admissions, emergency department visits, and mortality? What
25 other biomarkers of early effect may be used in the assessment of health effects?
- 26 • What evidence is available regarding the shape of concentration-response relationships
27 between short-term and long-term SO_x exposure and health effects?
- 28 • What evidence is available regarding the nature of health effects from the combination of
29 SO_x and other ambient air pollutants in comparison to health effects following exposure
30 to SO_x alone?
- 31 • What do results from studies conducted in environments near SO_x sources indicate about
32 the health effects of long-term or repeated SO_x exposures?
- 33 • To what extent does information across scientific disciplines on the pattern of SO_x
34 exposure (e.g., peak, repeated peak, average) provide understanding of the time course
35 for changes in health effects? What information is available on time-activity patterns of
36 study subjects such as time spent outdoors or activity levels that can aid in the
37 understanding of the nature of exposure or dosimetry of ambient SO_x concentrations that
38 are associated with health effects?
- 39 • To what extent do data across scientific disciplines provide information on health effects
40 related to various short-term SO_x exposure indices or averaging times relevant to the 1-
41 hour standard? What data exist comparing associations of health effects among various
42 short-term SO_x exposure metrics (e.g., 1-hour versus 24-hour)?

- 1 • What information is available regarding the effect of long-term, low-concentration
2 exposure to SO_x on an individual's sensitivity to short-term but higher concentration
3 exposures?
- 4 • What evidence is available regarding health effects related to long-term exposure
5 windows other than annual or lifetime average (e.g., preconception, pregnancy average)?
6 What data are available comparing associations of health effects among various long-
7 term SO_x exposure metrics (e.g., annual, seasonal, pregnancy average)? Are there critical
8 windows of human development that are associated with the development of chronic
9 respiratory disease?
- 10 • To what extent are the observed epidemiologic health effect associations attributable to
11 ambient SO_x, another ambient pollutant, or to the pollutant mixtures that SO_x may be
12 representing? To what extent do findings from experimental studies provide biological
13 plausibility?

14 E. Populations and Lifestyles Potentially at Increased Risk of SO_x-Induced Health Effects:

15 The 2008 SO_x ISA found substantial evidence from epidemiologic and controlled human
16 exposure studies that asthmatic individuals are more susceptible to respiratory health
17 effects from SO₂ exposures than the general public (U.S. EPA, 2008, section 5.4). The
18 ISA also presented limited evidence that children and older adults (≥ 65 years) are
19 potentially at increased risk of SO₂-induced respiratory effects. Since completion of the
20 2008 ISA, EPA has developed a framework to provide a consistent and transparent basis
21 for classifying the weight of evidence about whether populations and/or lifestyles are at
22 increased risk according to one of four levels: adequate evidence, suggestive evidence,
23 inadequate evidence, and evidence of no effect (see Table 5-1 of [ISA for Lead, U.S. EPA,](#)
24 [2013a](#)). In the framework, key considerations in drawing such conclusions include
25 consistency of findings for a factor within a discipline and coherence of the evidence
26 across disciplines. The current ISA will examine exposure and health outcome data to
27 draw conclusions about specific populations or lifestyles that are potentially at increased
28 risk of SO_x-induced health effects. Estimation of the sizes of potential populations and
29 lifestyles at increased risk and discussion of the public health significance of the health
30 outcomes characterized to result from ambient SO_x exposure may be included. Potential
31 populations or lifestyles at increased risk can be characterized by a variety of factors:
32 intrinsic factors (biological factors such as age, genetic variants), extrinsic factors
33 (nonbiological factors such as diet, lower socioeconomic status), and/or factors affecting
34 dose or exposure (age, outdoor activity or work). It is important to note that some factors

1 (e.g., age) are interconnected and may influence risk through multiple avenues. In the
2 current review, specific policy-relevant questions related to populations and lifestages
3 potentially at increased risk of SO_x-induced health effects that will be addressed include:

- 4 • Based on evidence integrated across studies and disciplines that examine factors which
5 may increase exposure to SO_x and/or risk of SO_x-induced health effects, what
6 conclusions can be drawn about the presence of at-risk lifestages (e.g., fetuses, children,
7 older adults) and/or populations?
- 8 • Studies from which disciplines contribute information about particular at-risk lifestages
9 and populations, and to what extent does limited or lack of information from specific
10 disciplines produce uncertainty in conclusions about at-risk lifestages and populations?
- 11 • How does new information augment that evaluated in the 2008 SO_x ISA regarding
12 populations with pre-existing respiratory disease or genetic variants as well as lifestages
13 potentially at increased risk of SO_x-induced health effects?
- 14 • What information is available that provides insight as to whether an at-risk lifestage or
15 population has higher exposure or dose of SO_x and/or has a greater biological response to
16 a given exposure?
- 17 • What is the extent of the coherence of evidence regarding potential at-risk lifestages or
18 populations for both short- and long-term exposures to SO_x?
- 19 • What quantitative information is available that characterizes the magnitude of greater
20 biological response or risk of health effects in at-risk lifestages or populations?

21 22 **4.5 SCIENTIFIC AND PUBLIC REVIEW**

23 Drafts of the ISA will be made available for review by the CASAC SO_x primary
24 NAAQS review panel and public as indicated in Figure 4-1 above; availability of draft
25 documents will be announced in the *Federal Register*. The CASAC panel will review the draft
26 ISA documents and discuss their comments in public meetings that will be announced in the
27 Federal Register. EPA will take into account comments, advice, and recommendations received
28 from the CASAC panel and from the public in revising draft ISA documents. EPA has
29 established a public docket for the development of the ISA. After appropriate revision based on
30 comments received from CASAC and the public, the final document will be made available on
31 an EPA website and in hard copy. A notice announcing the availability of the final ISA will be
32 published in the *Federal Register*.

5. QUANTITATIVE RISK AND EXPOSURE ASSESSMENTS

Within the context of NAAQS reviews, quantitative risk and exposure assessments (REAs) are designed to estimate human exposure and health risks associated with existing and potential alternative standards. The appropriate scope of any REA will be informed by the availability of scientific information from the ISA as well as air quality information and information on data and models that may help to address important uncertainties or provide additional insights beyond those provided by previous REAs. As a result, the first step in the REA planning process is an assessment of the appropriate scope of the REA, which includes a determination of whether a distinct REA document is needed. As part of this planning process, we evaluate the REA for the previous SO₂ NAAQS review in the context of the extent to which important uncertainties may be addressed by new information available since the previous review and the extent to which new information may change results of the REA in important ways or may allow for additional analyses that can address important gaps in our understanding of the exposures and risks associated with SO₂.

This phase of the NAAQS review begins with the preparation of a REA Planning Document and considers the extent to which newly available scientific evidence and tools/methodologies provide support for conducting quantitative risk and exposure assessments. To the extent warranted, the scope and methods for components of exposure/risk assessments will be described. As outlined in Table 2-1 above, the EPA plans to issue this REA Planning Document in February 2015. This document will be the subject of a CASAC consultation and will be made available to the public for review and comment. CASAC advice and public comments on this draft IRP will be considered in developing the REA Planning Document. If warranted, one or more drafts of an REA will then be prepared and released for CASAC review and public comment prior to completion of a final REA.

The information newly available in this review will be considered in light of the comprehensive, complex and resource-intensive quantitative assessments of human exposure and health risks documented in the 2009 REA as discussed in section 5.1 below. As discussed in section 5.2 below, the REA Planning Document will consider the available scientific evidence, tools and methodologies in light of areas of uncertainty identified in the 2009 REA and the potential for new analyses to provide notably different exposure and risk estimates, with lower associated uncertainty. CASAC advice and comments from the public on this draft IRP, as well as the availability of resources, will also inform development of the REA Planning Document.

5.1 OVERVIEW OF RISK AND EXPOSURE ASSESSMENT FROM PRIOR REVIEW

In the previous review of the primary SO₂ NAAQS, the REA focused the quantitative exposure and risk analyses on 5-minute levels of SO₂ in excess of potential health effect benchmark values derived from the controlled human exposure literature. These benchmark levels are not potential standards, but rather are concentrations which represent “exposures of potential concern” which are used in the analyses to estimate potential exposures and risks associated with 5-minute concentrations of SO₂. The health effect benchmark values used in the REA were derived primarily from the ISA’s evaluation of the 5 - 10 minute controlled human exposure literature. As noted above, the ISA concluded that moderate or greater decrements in lung function occurred in approximately 5 - 30% of exercising asthmatics following exposure to 200 - 300 ppb SO₂ for 5 - 10 minutes. In addition, the ISA concluded that moderate or greater decrements in lung function occurred in approximately 20 - 60% of exercising asthmatics following exposure to 400 - 600 ppb SO₂ for 5 - 10 minutes. The ISA also concluded that at SO₂ concentrations \geq 400 ppb, statistically significant moderate or greater decrements in lung function at the group mean level have often been reported and are frequently accompanied by respiratory symptoms. Moreover, small SO₂-induced lung function decrements have been observed in exercising asthmatics at concentrations as low as 100 ppb when SO₂ is administered via mouthpiece. Taken together, the REA concluded it was appropriate to examine potential 5-minute benchmark values in the range of 100 - 400 ppb.

The purpose of the assessments in the SO₂ REA was to characterize air quality, exposures, and health risks associated with recent ambient levels of SO₂, with SO₂ levels that could be associated with just meeting the then-existing SO₂ standards (i.e., 30 ppb annual average and 140 ppb daily average) and with SO₂ levels that could be associated with just meeting alternative 1-hour daily maximum standards. The SO₂ REA utilized three approaches to characterize health risks and are briefly described with the following.

In the first approach, measured 5-minute maximum SO₂ concentrations (1997 - 2007) from 98 ambient monitors were evaluated for exceedances of the 5-minute potential health effect benchmark levels, counting the number of days (per monitor and per year) a particular 5-minute benchmark concentration was exceeded and considering unadjusted, *as is* annual average, daily average, and 1-hour daily maximum SO₂ concentrations. In addition, 5-minute SO₂ maximum concentrations were statistically estimated³¹ using all available monitors that measured 1-hour

³¹The approach for statistically estimating 5-minute maximum concentrations from 1-hour concentrations was based on a characterization of ratios of measured 5-minute maximum concentrations to measured 1-hour average

1 SO₂ (1997 - 2006) to generate a similar output (i.e., the number of days per monitor per year a
2 benchmark concentration was exceeded considering as is air quality). Then, 5-minute maximum
3 concentrations were statistically estimated in 40 selected U.S. counties (2001 - 2006), though
4 using 1-hour SO₂ concentrations *as is* and, those adjusted to just meet the then-existing annual
5 and daily standards, and concentrations adjusted to just meet potential 1-hour daily maximum
6 alternative standards. In this analysis, all U.S. monitoring sites where SO₂ data have been
7 collected were included in this analysis and, as such, the results generated were considered a
8 broad characterization of national air quality and potential human exposures that might be
9 associated with these concentrations.

10 In the second approach, we used EPA's Air Pollutants Exposure (APEX) model (US
11 EPA, 2012a,b), a Monte Carlo simulation model that can be used to simulate a large number of
12 randomly sampled individuals within specified locations, generating estimates of population
13 exposure. APEX simulates exposures in indoor, outdoor, and in-vehicle microenvironments
14 while taking into consideration the movement of individuals through time and space. APEX
15 estimated 5-minute daily maximum exposures simulated asthmatics may experience while at
16 moderate or greater exertion (e.g., while exercising) and compared these exposures to the same
17 5-minute potential health effect benchmark levels. Two case study areas were selected for this
18 exposure modeling: Greene County, Missouri, and three counties within the St. Louis
19 Metropolitan Statistical Area (MSA). For these two case study areas, year 2002 census block-
20 level hourly SO₂ concentrations were estimated by EPA's AERMOD (a dispersion model), input
21 to APEX and combined with the same statistical model used for estimating 5-minute peaks
22 described from the hourly SO₂ concentrations above. Several modeled air quality scenarios were
23 considered, including *as is* air quality, air quality adjusted to just meet the then-existing
24 standards, and air quality adjusted to just meet potential alternative 1-hour daily maximum
25 standards. Output from this exposure modeling were the number and percent of asthmatics in
26 each study area experiencing at least one 5-minute daily maximum exposure at or above the
27 potential health effect benchmark levels while at moderate or greater exertion.

28 In the third approach, exposure-response relationships derived from controlled human
29 exposure studies were used in conjunction with the outputs of the St. Louis and Greene County
30 exposure analysis to estimate health impacts. More specifically, in each location we estimated
31 the number and percent of all asthmatics or asthmatic children at moderate or greater exertion
32 expected to experience moderate or greater decrements in lung function defined in terms of sRaw
33 or FEV₁ and considering the same air quality scenarios mentioned above.

concentrations (Section 7.2.3 of the 2009 SO₂ REA). Nineteen separate ratio distributions were developed from the measurement data, stratified by seven 1-hour concentration levels and three concentration variability levels.

1 As mentioned above for each of these approaches, ambient SO₂ concentrations and
2 exposures were characterized by considering *as is* air quality (unadjusted concentrations) and
3 several hypothetical air quality scenarios. Each of the hypothetical air quality scenarios had an
4 ambient concentration target, derived from the form and level of the then-existing NAAQS or
5 from potential alternative standards. Staff chose a proportional approach to adjust the SO₂
6 concentrations to simulate each of the current and alternative air quality standard scenarios. A
7 proportional approach was selected based on the mostly linear relationship between older high
8 concentration years of air quality when compared with recent low concentration years at several
9 locations (2009 SO₂ REA, Section 7.4.2.5).

10 The approach used to evaluate uncertainty was adapted from guidelines outlining how to
11 conduct a qualitative uncertainty characterization (WHO, 2008), though staff also performed
12 several quantitative sensitivity analyses to iteratively inform both model development and the
13 qualitative uncertainty characterization, where possible. While it may be considered ideal to
14 follow a tiered approach in the REA to quantitatively characterize all identified uncertainties,
15 staff selected the mainly qualitative approach given the limited data available to inform
16 probabilistic analyses and time and resource constraints.

17 The following identifies the key observations and uncertainties from the prior SO₂ REA.
18

19 **5.1.1 Key Observations**

20 **Ambient Air Quality Characterization**

- 21 • An increased probability of any 5-minute benchmark exceedance was consistently related
22 to either increased 24-hour average or 1-hour daily maximum concentrations.
- 23 • For any of the air quality scenarios considered, the probability of exceeding the 5-minute
24 maximum benchmark levels was consistently greater at monitors sited in low-population
25 density areas compared with high-population density areas.
- 26 • Unadjusted *as is* air quality at ambient monitors measuring 5-minute maximum
27 concentrations:
 - 28 ○ Measured daily and annual average concentrations were below that of the existing
29 standards at all monitors, though measured 5-minute maximum ambient
30 concentrations were present above the potential health effect benchmark levels.
31 (2009 SO₂ REA, Appendix A, Table A.5-1)
 - 32 ■ Nearly 70% of the monitor site-years analyzed had at least one daily 5-
33 minute maximum concentration above 100 ppb and over 20% had \geq 25
34 days with a daily 5-minute maximum concentration above 100 ppb.
 - 35 ■ About 44% of the monitor site-years analyzed had at least one 5-minute
36 daily maximum concentration > 200 ppb, 25% had at least one > 300 ppb,
37 and 17% had at least one > 400 ppb.
 - 38

- 1 • Air quality adjusted to simulate just meeting the then-existing annual standard in the 40
2 selected U.S. counties
 - 3 ○ All counties evaluated were estimated to have multiple days per year where 5-
4 minute daily maximum ambient SO₂ concentrations are > 100 ppb. For example,
5 most counties are estimated to have, on average, 100 days or more per year with
6 5-minute daily maximum SO₂ concentrations > 100 ppb (2009 SO₂ REA, Table 7-
7 11).
 - 8 ○ Fewer benchmark exceedances were estimated to occur with higher benchmark
9 levels. For example, five of the forty counties were estimated to have 60 or more
10 days per year with 5-minute maximum SO₂ concentrations that exceed 300 ppb
11 (2009 SO₂ REA, Table 7-13).
- 12 • Air quality adjusted to potential 1-hour daily maximum alternative standard levels:
 - 13 ○ Far fewer days per year with 5-minute maximum SO₂ concentrations > 300 ppb
14 and > 400 ppb (about 0 to 5 days/year) were estimated when adjusting air quality
15 to just meet potential alternative standard levels of 100 and 150 ppb than
16 compared with air quality adjusted to just meet the current standards (frequently
17 25 or more days/year) and the potential alternative standard levels of 200 and 250
18 ppb (about 5 to 20 days/year) (2009 SO₂ REA, Tables 7-13 and 7-14).

19 Exposure Assessment

- 20 • St. Louis had both a greater number and percent of asthmatic children and adults exposed
21 above the benchmark levels than did Greene County for all air quality scenarios, largely a
22 function of both the greater population density and the much greater SO₂ emissions
23 density in St. Louis (2009 SO₂ REA, Section 8.9.2).
- 24 • Estimated exposures above 5-minute potential health effect benchmark levels at moderate
25 or greater exertion using APEX occurred most frequently outdoors (around 50 to > 90%,
26 depending on the air quality scenario and modeling domain) (2009 SO₂ REA, Figure 8-
27 21).
- 28 • Simulating air quality that just meets the then-existing annual standard in either the
29 Greene County or St. Louis Study areas resulted in the greatest number and percent of
30 asthmatic persons exposed at all benchmark levels (2009 SO₂ REA, Figures 8-16 and 8-
31 19).
- 32 • The exposure results using *as is* air quality were similar to that estimated using air quality
33 adjusted to a 99th percentile 1-hour daily maximum of 50 or 100 ppb in either study area
34 (2009 SO₂ REA, Figures 8-16 and 8-19).

35 Health Risk Assessment

- 36 • In terms of estimated percentage of all asthmatics or asthmatic children experiencing one
37 or more lung function responses, estimated risks are greater for asthmatic children (2009
38 SO₂ REA, Tables 9-5 and 9-8, respectively), likely because they spend more time
39 outdoors and at higher exertion levels than adults.
 - 40 ○ For example, approximately 13% of all asthmatics were estimated to experience
41 at least one moderate lung function response (defined as an increase in sRaw \geq

1 100% (2009 SO₂ REA, Table 9-5), while approximately 19% of asthmatic
2 children experienced a similar response (2009 SO₂ REA, Table 9-8).

- 3 • A broad range of SO₂ exposure concentration intervals selected, some as high as 500 ppb,
4 contributes to the estimated risks of experiencing one or more lung function responses
5 per year for some of the standards considered in the assessment. For potential alternative
6 1-hour standards in the range of 100 to 150 ppb, SO₂ exposure concentration intervals
7 below 200 ppb contribute to most of the estimated risks of experiencing one or more lung
8 function responses per year (2009 SO₂ REA, Figures 9-7 and 9-8).

10 **5.1.2 Key Uncertainties**

- 11 • Uncertainty in the statistical model used to estimate 5-minute maximum SO₂
12 concentrations from 1-hour SO₂ concentrations.
- 13 • Uncertainty in the spatial and temporal representativeness of the SO₂ ambient monitoring
14 network.
- 15 • Uncertainties associated with the proportional air quality adjustment procedure that was
16 used to simulate just meeting the then-existing standard and several alternative 1-hour
17 daily maximum standards.
- 18 • Uncertainties related to the exposure model inputs and exposure estimates which are an
19 important input to the risk assessment.
- 20 • Uncertainty about the shape of the exposure-response relationship for lung function
21 responses at levels well below 200 ppb, the lowest level examined in free-breathing
22 single-pollutant controlled human exposure studies.
- 23 • Uncertainty with respect to how well the estimated exposure-response relationships
24 reflect asthmatics with more severe disease than those tested in chamber studies.
- 25 • Uncertainty about whether the presence of other pollutants in the ambient air would
26 enhance the SO₂-related responses observed in the controlled human exposure studies.
- 27 • Uncertainty about the extent to which the risk estimates presented for the two modeled
28 areas in Missouri are representative of other locations in the U.S. with significant SO₂
29 point and area sources.

31 **5.2 CONSIDERATION OF QUANTITATIVE ASSESSMENTS FOR THIS** 32 **REVIEW**

33 This discussion is focused particularly on considering the extent to which newly available
34 scientific evidence and tools/methodologies are available to inform our understanding of the key
35 areas of uncertainty identified in the 2009 REA. As outlined in Table 2-1 above, the EPA plans
36 to release an REA Planning Document for consultation with CASAC and for public comments in
37 February 2015 that will consider the extent to which new quantitative risk and exposure
38 assessments would be appropriate to conduct in the current review. CASAC review and public
39 comments on this draft IRP will be considered in developing the REA Planning Document.

1 Some key areas being considered by staff, including types of data, methodologies and
2 tools, are identified and summarized below, with a focus on the three approaches used to
3 estimate exposure and health risk: an air quality characterization, an exposure assessment, and a
4 health risk assessment.

5 **5.2.1 Ambient Air Quality Characterization**

6 The goals of an SO₂ ambient air quality characterization in a new quantitative risk and
7 exposure assessment would be (1) to estimate short- and long-term ambient concentration levels
8 that consider unadjusted SO₂ air quality and air quality adjusted to just meeting the existing and
9 any potential alternative SO₂ standards; (2) to develop quantitative relationships between short-
10 term peak concentrations and time-averaged concentrations; and (3) to identify key assumptions
11 and uncertainties.

12 For the analyses conducted during the last review, ambient SO₂ monitoring data were
13 available up to mid-2007 (2006 was the most recent year with complete data at that time). Since
14 that review, additional 5-minute data have become available (Table 5-1), particularly during the
15 most recent years (2010-2012). Ambient monitors reporting all twelve 5-minute values per hour
16 are tabulated in the 2nd column; monitors which report one maximum 5-minute value per hour
17 are in the 3rd column; and hourly average monitors not included in the two preceding columns
18 are counted in the last column. Given the greatly expanded number of monitors, it is possible
19 that we could develop a new statistical model to estimate 5-minute concentrations from hourly
20 concentrations. Additional ambient monitoring attributes (e.g., proximity to selected emission
21 sources) could be considered in its design. Output from this new model could be compared with
22 that generated using the statistical model used in the prior air quality characterization. In
23 addition, relationships between 5-minute peak concentrations and longer averaging times (e.g.,
24 greater than 1-hour but less than 24-hour) would be considered. And finally, new completeness
25 criteria could be proposed in development of this new statistical model to potentially ensure the
26 quality and representativeness of available measurements that are used.

27 Table 5-2 summarizes the potential areas where additional information, if available,
28 would provide reasonable substance to address key uncertainties identified in the previous
29 review. These will be considered, in addition to the above factors, in deciding the extent to
30 which new quantitative risk and exposure assessments would be appropriate to conduct in the
31 current review.

Table 5-1. The numbers of SO₂ monitors 2003 to 2012³²

Year	Monitors Reporting 5-Minute Continuous Concentrations ¹	Monitors Reporting 5-Minute Maximum Concentrations ²	Monitors Reporting 1-Hour Concentrations ²
2003	6	40	528
2004	6	32	524
2005	6	24	510
2006	4	24	498
2007	4	22	499
2008	3	20	471
2009	2	20	440
2010	149	31	435
2011	194	183	435
2012	195	185	450

¹ 5-minute continuous monitors with at least 20,000 values/year (about 20% data completeness).

² 5-minute maximum and hourly with at least 50% data completeness (4,380 values/year).

5.2.2 Exposure Assessment

The goals of an SO₂ exposure assessment in a new quantitative risk and exposure assessment would be (1) to estimate short- and long-term exposures to ambient concentrations through air quality and modeling analyses considering current air quality for SO₂ and air quality levels just meeting the current and any potential alternative SO₂ standards; (2) compare estimated exposures to potential health effect benchmark levels; and (3) to identify key assumptions and uncertainties. Our assessment of uncertainties in the prior SO₂ REA and the potential utility and impact of newly available information regarding the conduct of a new exposure assessment could consider the following:

- Factors that may contribute to greater personal exposures including the impacts of important sources of SO₂ (e.g., outdoor point sources).
- Factors that may contribute to lessened personal exposures including infiltration and the decay of SO₂ indoors.
- 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 or otherwise living in areas with elevated SO₂ concentrations.
- Frequency and (temporal and spatial) variability of peak air quality levels at concentrations and averaging times of significance.

³² In the last review, the final rulemaking required States to report either the highest 5-minute concentration for each hour of the day, or all twelve 5-minute concentrations for each hour of the day (see section 1.3)

1 As done was done previously, APEX could be used though we would employ the latest
2 version the model³³ (US EPA, 2012a; 2012b) to estimate 5-minute or long-term exposures of
3 interest. Table 5-2 summarizes the potential areas where additional information regarding the
4 assessment of exposure, if available, would provide reasonable substance to address key
5 uncertainties identified in the previous review. These will be considered, in addition to the
6 above factors, in deciding the extent to which new quantitative risk and exposure assessments
7 would be appropriate to conduct in the current review.

8 **5.2.3 Risk Assessment**

9 The goals of a SO₂ risk assessment in a new quantitative risk and exposure assessment
10 would be (1) to estimate the number/percent of people at risk of adverse health effects following
11 exposure to SO₂ concentrations considering current air quality for SO₂ and air quality levels just
12 meeting the current and any potential alternative SO₂ standards; (2) to provide distributions of
13 health risk estimates over a range of ambient SO₂ concentrations; and (3) to identify key
14 assumptions and uncertainties. Our assessment of uncertainties in the prior SO₂ REA and the
15 potential utility and impact of newly available information regarding the conduct of a new risk
16 assessment could consider the following:

- 17 • The level and averaging time associated with potential health effect benchmark levels,
18 particularly if there are newly identified at-risk study groups.
- 19 • New controlled human exposure studies having the same responses reported in the last
20 review (i.e., sRaw and FEV₁) or newly identified adverse responses that could form the basis
21 for the development of exposure-response (E-R) relationships.
- 22 • New epidemiologic study(s) that provide(s) concentration-response (C-R) relationships based
23 on data collected in environmentally-relevant settings. Depending on the type of health
24 response function(s) available, ambient SO₂ concentration data would be used for
25 characterizing risks and would be most appropriately applied in areas where the
26 epidemiologic study was performed.

27
28 Table 5-2 summarizes the potential areas where additional information regarding the
29 assessment of risk, if available, would provide reasonable substance to address key uncertainties
30 identified in the previous review. These will be considered, in addition to the above factors, in
31 deciding the extent to which new quantitative risk and exposure assessments would be
32 appropriate to conduct in the current review.

³³ APEX is also referred to as the Total Risk Integrated Methodology/Exposure (TRIM.Expo) model (see http://www.epa.gov/ttn/fera/trim_gen.html for general details on TRIM).

1 **Table 5-2. Primary uncertainties associated with the exposure and risk assessments in the**
 2 **previous review and the potential use of new information for reducing these uncertainties**

Component of Assessment	Uncertainty/Limitation Remaining From Prior REA	Consideration of Potential Utility of Information Newly Available in This Review For the Assessment
Air quality characterization		
Characterize relationships between 5-minute peak concentrations and longer averaging times.	Ambient monitor spatial and temporal representativeness regarding the limited number of monitors reporting 5-minute SO ₂ concentrations.	There are now more monitors reporting 5-minute concentrations compared with that used in the last review.
Develop predictive relationships to approximate the probability of occurrence of 5-minute peak concentrations given hourly average concentrations and site specific data for use in locations without 5-minute ambient monitors.	Uncertainty of the statistical model used to estimate 5-minute maximum SO ₂ concentrations at monitors that reported only 1-hour SO ₂ concentrations.	A new characterization of monitor site attributes and emissions sources influencing both 5-minute and hourly SO ₂ ambient monitoring concentrations could be performed.
The estimated number of exceedances of potential health effect benchmark levels occurring at monitors located across the U.S.	Ambient monitor spatial and temporal representativeness	
Selection of potential health effect benchmark levels	<p>The health effect benchmark levels used in the SO₂ REA were derived from the ISA's evaluation of the 5 - 10 minute controlled human exposure literature.</p> <p>The subjects participating in these human exposure studies were exercising asthmatics and do not include individuals who may be most susceptible to the respiratory effects of SO₂ (e.g., the most severe asthmatics).</p> <p>Since the majority of controlled human exposure studies investigating lung function</p>	New estimates of benchmark exceedances could be developed if there are studies newly available that indicate alternative benchmark levels exist outside of the range already considered in the 2009 SO ₂ REA.

Component of Assessment	Uncertainty/Limitation Remaining From Prior REA	Consideration of Potential Utility of Information Newly Available in This Review For the Assessment
	responses to SO ₂ were conducted with adult subjects, the risk assessment relies on data from adult asthmatic subjects to estimate exposure-response relationships that have been applied to all asthmatic individuals, including children.	
Approach used to simulate just meeting potential air quality standard scenarios	The proportional adjustment factors derived from an area's design monitor are applied to adjust all ambient monitors within the given study area. Deviation from proportionality at any monitor could result in either over or under-estimation of concentrations.	A different methodology could be used if there are studies newly available that indicate an improved alternative approach to adjusting air quality.
Exposure assessment		
The estimated number of people with exposures above the potential health effect benchmarks in different locations	Uncertainty in some of the exposure model input data (e.g., activity patterns, indoor decay rates, air exchange rates)	It is possible that there could be additional data and/or analyses that could be reduce this uncertainty to some extent.
Representativeness of study areas	The modeling approach used in the prior REA to assessing exposures was resource intensive; therefore, the geographic scope of this analysis was limited to two study areas, albeit having two differing emissions and population densities.	The availability of recently collected 5-minute ambient monitor concentrations and consideration of other air quality input data sources (e.g., dispersion model) could allow for exposure estimates to be developed in other study areas.
Risk assessment based on clinical exposure studies		
Probabilistic exposure-response relationships	A generally common and important uncertainty in human exposure studies is the limited number of study subjects as well as limits to the type of pre-existing health conditions subjects may have, particularly if the health condition affords the subject with heightened	The availability of new clinical studies could reduce the uncertainty associated with probabilistic exposure-response relationships.

Component of Assessment	Uncertainty/Limitation Remaining From Prior REA	Consideration of Potential Utility of Information Newly Available in This Review For the Assessment
	<p>effects sensitivity to the pollutant exposure.</p> <p>There remains greater uncertainty in responses below 200 ppb because of the lack of experimental data.</p>	
Risk assessment based on epidemiologic studies		
City-specific concentration-response relationships	In the last SO ₂ NAAQS review, the REA concluded that the epidemiologic evidence was not appropriate for use in quantitative risk analyses.	<p>The ability to conduct an epidemiology-based risk assessment for SO₂ would depend on the availability of concentration-response relationships from new epidemiologic studies sufficient to reduce the uncertainty to an acceptable level.</p> <p>A risk characterization based on epidemiologic studies also requires baseline incidence rates and population data for the risk assessment locations.</p>

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5.2.4 Uncertainty and Variability

The uncertainty and variability inherent in characterizing ambient air quality and in estimating exposure and risk would also be evaluated in a new quantitative risk and exposure assessment. 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). Consistent with prior NAAQS REAs including the last SO₂ REA, EPA would consider using the approach described in WHO (2008), whereas 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.

5.3 PUBLIC AND SCIENTIFIC REVIEW

The CASAC review panel on the SO₂ primary NAAQS will be consulted on the risk/exposure assessment REA Planning Document at a public meeting. The panel will also review drafts of the risk/exposure assessment. 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 SO₂, 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. AMBIENT AIR MONITORING

In the course of NAAQS reviews, aspects of the methods for measuring ambient levels of the NAAQS pollutant, as well as the current network of monitors, including their physical locations and monitoring objectives, are reviewed. The methods for sampling and analysis of each NAAQS pollutant are generally reviewed in conjunction with consideration of the indicator element for each NAAQS. Consideration of the ambient air monitoring network generally informs the interpretation of current data on ambient air concentrations and includes an assessment of the adequacy of the monitoring network for determining compliance with the existing or, as appropriate, a potentially revised NAAQS. This chapter describes plans for considering these aspects of the ambient air monitoring program for sulfur oxides which includes the indicator SO₂.

6.1 CONSIDERATION OF SAMPLING AND ANALYSIS METHODS

In order for the data to be used to determine compliance, ambient SO₂ concentration data must be obtained using Federal Reference Methods (FRMs) or Federal Equivalent Methods (FEMs) which are designated by the Agency in accordance with 40 CFR Part 50 and Part 53. As described earlier, SO₂ is the indicator for the sulfur oxides NAAQS, and has been routinely measured by UV fluorescence FEMs since the 1980s. The SO₂ concentration data produced by modern FEM analyzers are routinely logged by state and local agencies whom report the hourly average and either the maximum 5-minute value (one of twelve 5-minute periods) in the hour or all twelve 5-minute averages within the hour to EPA's Air Quality System (AQS).

The Agency is unaware of any recent technological advances in SO₂ measurements or forthcoming modifications to existing methods that should be considered in this NAAQS review. Therefore, the EPA does not anticipate raising any specific sampling and analysis methods issues for consideration in this integrated review plan.

6.2 CONSIDERATION OF AIR MONITORING NETWORK REQUIREMENTS

The ambient air quality monitoring networks for criteria pollutants support three major objectives: (1) to provide air pollution data to the general public in a timely manner; (2) to

1 support compliance with NAAQS and emissions strategy development; and (3) to support air
2 pollution research studies. A review of the available SO₂ monitoring network and data was
3 performed as part of the primary SO₂ NAAQS review completed in 2010. Subsequent to that
4 review, and in conjunction with revising the primary standards, the Agency promulgated
5 minimum monitoring requirements to support the implementation of a new primary 1-hour SO₂
6 standard. The 2010 action introduced minimum requirements based upon the use of a Population
7 Weighted Emissions Index (PWEI). The PWEI utilizes both population and emissions data
8 within Core Based Statistical Areas (CBSAs) to determine if monitoring is required in a CBSA
9 and, if so, how many monitors are required. The intent of using the PWEI to require monitors is
10 to focus monitoring into areas where there is a higher proximity of population and SO₂
11 emissions. In effect, areas with a higher calculated PWEI value are expected to have higher
12 potential for population exposure to peak, short-term SO₂ emissions.

13 Historically, the data used to determine compliance with the SO₂ NAAQS have been
14 largely based upon data obtained from ambient monitors operated by state, local, and tribal air
15 monitoring agencies. These monitors are either required due to federal regulation contained in
16 40 CFR Part 58, Appendix D, state implementation plans, industrial permits, or other state or
17 local requirements or voluntary actions. While monitoring data are a mainstay in determining
18 compliance for all other criteria pollutants, SO₂ is unique in that there is a precedent to also use
19 dispersion modeling in the implementation of its NAAQS. This is notable because the use of
20 modeling in lieu of monitoring can potentially reduce the necessary size and distribution of a
21 compliance monitoring network. As a result, the final monitoring requirements promulgated as
22 part of the 2010 SO₂ NAAQS revision reflected this potentiality.³⁴

23 As of December 2013, the ambient SO₂ monitoring network is estimated to have 431
24 monitors in operation nationwide. This number far exceeds the approximate 129 required by
25 PWEI.

³⁴ The best available rationale and description of the Agency's current thinking on the SO₂ implementation is "Next Steps for Area Designations and Implementation of the Sulfur Dioxide National Ambient Air Quality Standard," also known as the "strategy paper," which was released in February of 2013 (<http://www.epa.gov/airquality/sulfurdioxide/pdfs/20130207SO2StrategyPaper.pdf>).

7. POLICY ASSESSMENT/RULEMAKING

7.1 POLICY ASSESSMENT

The PA, like the previous OAQPS Staff Paper, is a document that provides a transparent OAQPS staff analysis and staff conclusions regarding the adequacy of the current standard and potential alternatives that are appropriate to consider prior to the issuance of proposed and final rules. The PA integrates and interprets the information from the ISA and REA(s) to frame policy options for consideration by the Administrator. The PA is also intended to facilitate CASAC's advice to the Agency and recommendations to the Administrator on the adequacy of the existing standard or revisions that may be appropriate to consider. Staff conclusions in the PA are based on the information contained in the ISA and, as available, the REA, and any additional staff evaluations and assessments discussed in the PA. In so doing, the discussion in the PA is framed by consideration of a series of policy-relevant questions drawn from those outlined in chapter 3, including the fundamental questions associated with the adequacy of the current standard and, as appropriate, consideration of an alternative standard(s) in terms of the specific elements of the standard: indicator, averaging time, level, and form.

The PA for the current review will identify conceptual evidence-based and risk/exposure-based approaches for reaching public health policy judgments. It will discuss the implications of the science and quantitative assessments for the adequacy of the current primary standard and for any alternative standards under consideration. The PA will also describe a broad range of policy options for standard setting, identifying the range for which the staff identifies support within the available information. In so doing, the PA will describe the underlying interpretations of the scientific evidence and risk/exposure information that might support such alternative policy options that could be considered by the Administrator in making decisions for the primary SO₂ standard. Additionally, the PA will identify key uncertainties and limitations in the underlying scientific information and in our assessments. The PA will also highlight areas for future health-related research, model development, and data collection.

In identifying a range of primary standard options for the Administrator to consider, it is recognized that the final decision will be largely a public health policy judgment. A final decision must draw upon scientific information and analyses about health effects and risks, as well as judgments about how to deal with the range of uncertainties that are inherent in the scientific evidence and analyses. Staff's approach to informing these judgments recognizes that the available health effects evidence generally reflects a continuum consisting of ambient concentrations at which scientists generally agree that health effects are likely to occur, through lower concentrations at which the likelihood and magnitude of the response become increasingly

1 uncertain. This approach is consistent with the requirements of the NAAQS provisions of the
2 CAA and with how the EPA and the courts have historically interpreted the Act. These
3 provisions require the Administrator to establish primary standards that are requisite to protect
4 public health and are neither more nor less stringent than necessary for this purpose. As
5 discussed in section 1.1 above, the provisions do not require that primary standards be set at a
6 zero-risk level, but rather at a level that avoids unacceptable risks to public health, including the
7 health of at-risk populations³⁵.

8 Staff will prepare at least one draft of the PA document for CASAC review and public
9 comment. The draft PA document will be distributed to the CASAC Sulfur Oxides Primary
10 NAAQS Review Panel for their consideration and provided to the public for review and
11 comment. Review by the CASAC Panel will be discussed at public meetings that will be
12 announced in the *Federal Register*. Based on past practice by CASAC, the EPA expects that
13 CASAC would summarize their key advice and recommendations for revision of the document
14 in a letter to the EPA Administrator. In revising the draft PA document, OAQPS will take into
15 account any such recommendations, and also consider comments received from CASAC and
16 from the public, at the meeting itself, and any written comments received. The final document
17 will be made available on an EPA website, with its public availability announced in the *Federal*
18 *Register*.

20 **7.2 RULEMAKING**

21 Following issuance of the final PA and the EPA management consideration of staff
22 analyses and conclusions presented therein, and taking into consideration CASAC advice and
23 recommendations, the Agency will develop a notice of proposed rulemaking. The proposed
24 rulemaking notice conveys the Administrator’s proposed conclusions regarding the adequacy of
25 the current standard(s) and any revision that may be appropriate. A draft notice of proposed
26 rulemaking will be submitted to the Office of Management and Budget (OMB) for interagency
27 review, in which OMB and other federal agencies are provided the opportunity for review and
28 comment. After the completion of interagency review, the EPA will publish the notice in the
29 *Federal Register* seeking comment on proposed agency action – namely whether or not to revise
30 the current standard, and if so, how. Monitoring rule changes associated with review of the

³⁵ The at-risk population groups identified in a NAAQS review may include low income or minority groups. Where low income/minority groups are among the at-risk populations, the rulemaking decision will be based on providing protection for these and other at-risk populations and lifestages (e.g., children, older adults, persons with pre-existing heart and lung disease). To the extent that low income/minority groups are not among the at-risk populations identified in the ISA, a decision based on providing protection of the at-risk lifestages and populations would be expected to provide protection for the low income/minority groups.

1 primary SO₂ standard, and drawing from considerations outlined in Chapter 6 above, will be
2 developed and proposed, as appropriate, in conjunction with this NAAQS rulemaking.

3 At the time of publication of the notice of proposed rulemaking, all materials on which
4 the proposal is based are made available in the public docket for the rulemaking.³⁶ Publication
5 of the proposal notice is followed by a public comment period, generally lasting 60 to 90 days,
6 during which the public is invited to submit comments on the proposal to the rulemaking docket.
7 EPA also will provide opportunity for a public hearing on any proposed action. Taking into
8 account comments received on the proposed action, the Agency will then develop a notice of
9 final rulemaking, which again undergoes OMB-coordinated interagency review prior to issuance
10 by the EPA of the final rule. At the time of final rulemaking, the Agency responds to all
11 significant comments on the proposed action.³⁷ Publication of the final action in the *Federal*
12 *Register* completes the process.

³⁶ The rulemaking docket for the current primary SO₂ NAAQS review is identified as EPA-HQ-OAR-2013-0566. This docket has incorporated the ISA docket (EPA-HQ-ORD-2013-0357) by reference. Both dockets are publicly accessible at www.regulations.gov.

³⁷ For example, Agency responses to all substantive comments on the 2009 notice of proposed rulemaking in the last review were provided in the preamble to the final rule and in a document titled *Responses to Significant Comments on the 2009 Proposed Rule on the Primary National Ambient Air Quality Standards for Sulfur Dioxide*, available at: http://www.epa.gov/ttn/naaqs/standards/so2/s_so2_cr_rc.html

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APPENDIX A

DRAFT OUTLINE FOR INTEGRATED SCIENCE ASSESSMENT FOR SULFUR OXIDES – HEALTH CRITERIA

Preamble (will be available online)	Process of ISA Development EPA Framework for Causal Determination Public Health Impact Concepts in Evaluating Adversity of Health Effects
Preface	Legislative Requirements for the NAAQS Review History of the Primary NAAQS for Sulfur Dioxide
Executive Summary	
Chapter 1	Integrative Summary
1.1	Policy-relevant Questions for Sulfur Dioxide NAAQS Review
1.2	ISA Development and Scope
1.3	Sulfur Oxides Sources, Ambient Concentrations, Exposure
1.4	Health Effects Evidence Exposure, Dosimetry, and Modes of Action Comparison of 2008 ISA and Current Conclusions Key Evidence for Evaluated Health Effects
1.5	Policy-Relevant Considerations Concentration-Response and Thresholds Exposure Averaging Times and Lags At-risk Populations Adverse Health Effects, Public Health Significance
1.6	Summary
Chapter 2	Atmospheric Behavior of Sulfur Oxides
2.1	Introduction
2.2	Sources
2.3	Atmospheric Chemistry and Fate
2.4	Monitoring
2.5	Atmospheric Concentrations of Sulfur Oxides
2.6	Modeling
2.7	Summary and Conclusions
Chapter 3	Exposure to Ambient Sulfur Oxides
3.1	Introduction
3.2	General Considerations
3.3	Exposure Measurement
3.4	Exposure-related Metrics

3.5	Exposure Modeling
3.6	Implications for Epidemiologic Studies
3.7	Summary and Conclusions
Chapter 4	Integrated Health Effects Exposure to Sulfur Oxides
4.1	Introduction
4.2	Dosimetry and Mode of Action
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4.4	Cardiovascular Morbidity (Short-Term and Long-Term)
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