Review of the Primary National Ambient Air Quality Standard for Sulfur Oxides:

Risk and Exposure Assessment Planning Document

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Review of the Primary National Ambient Air Quality Standard for Sulfur Oxides:

Risk and Exposure Assessment Planning Document

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Office of Air Quality Planning and Standards
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LIST OF ACRONYMS AND ABBREVIATIONS

APEX	Air Pollutants Exposure model
AQS	Air Quality System
BSA	body surface area
CAA	Clean Air Act
CASAC	Clean Air Scientific Advisory Committee
CHAD	Consolidated Human Activity Database
EGU	Electricity generating unit
EPA	Environmental Protection Agency
EVR	equivalent ventilation rate
FEV_1	forced expiratory volume in one minute
FR	Federal Register
IRP	Integrated Review Plan
ISA	Integrated Science Assessment
ME	microenvironment
MET	metabolic equivalent of task
MSA	metropolitan statistical area
NAAQS	National Ambient Air Quality Standard
NEI	National Emissions Inventory
NHANES	National Health and Nutrition Examination Survey
NHIS	National Health Interview Survey
NO_2	nitrogen dioxide
O_3	ozone
OAQPS	Office of Air Quality Planning and Standards
ppb	parts per billion
PA	Policy Assessment
PM	particulate matter
PMR	peak-to-mean ratio
PRB	policy-relevant background
REA	Risk and Exposure Assessment
RMR	resting metabolic rate
SO_2	sulfur dioxide
SO_X	oxides of sulfur
sRaw	specific airway resistance
$\dot{V}_E$	activity-specific ventilation rate

EXECUTIVE SUMMARY

The U.S. Environmental Protection Agency (EPA) is conducting a review of the air quality criteria and the primary (health-based) national ambient air quality standard (NAAQS) for sulfur oxides as described in the 2014 *Integrated Review Plan for the Primary National Ambient Air Quality Standard for Sulfur Dioxide*. Based on analysis of the information available in this review with regard to support for a quantitative risk and exposure assessment (REA) to inform the review, this document outlines a plan, including scope and methods, for a REA. The information considered includes the currently available scientific evidence, as assessed in the second draft *Integrated Science Assessment for Sulfur Oxides – Health Criteria* (ISA), relevant tools or methodologies, and other information or data, including that which is newly available in this review.

As in the last review of the primary sulfur dioxide (SO_2) standards, which was completed in 2010, the health effects evidence available in this review indicates that short-term exposures are causally linked to respiratory effects and that people with asthma are the at-risk population. Specifically, controlled human exposure studies demonstrate an increased risk of lung function decrements for people with asthma exposed while at increased ventilation rates. The plan for the REA is based on these findings. This is similar to the REA conducted as part of the last review (2009 REA), which included quantitative analyses of both exposure and risk. Specifically, the 2009 REA included: analyses focused on short-term (5-minute) SO_2 concentrations; an exposure assessment designed to estimate exposures likely to be experienced by at-risk populations while at increased ventilation; and risk characterization utilizing two types of metrics: (1) comparisons of exposures to concentrations of potential concern (benchmark levels), and (2) lung function risk estimates.

This document and the planned quantitative analyses reflect several important new pieces of information that can be used to address areas of uncertainty in the last review. Perhaps most importantly, the plan for the REA outlined in this document focuses on the updated SO_2 air monitoring dataset available in this review. Specifically, the data for 5-minute concentrations are greatly expanded with regard to both the number of monitoring locations for which hourly maximum 5-minute concentrations are available and the number for which all 5-minute values for each hour are available. Limitations in the 5-minute dataset available at the time of the last review influenced the approaches that could be used in the 2009 REA to characterize the potential for at-risk populations to experience exposures of potential concern. The analysis approach for the new REA will be based on linking the health effects information to population exposure estimates that draw on this improved understanding of 5-minute concentrations of SO_2

in the ambient air and will also take advantage of a number of improvements and updates to the air quality, exposure, and risk models, and associated input data.

As in the last review, EPA intends to use the Air Pollutant Exposure model (APEX) to estimate population exposures that account for the time people spend in different microenvironments, as well as for time spent at elevated ventilation rates while exposed to peak 5-minute SO_2 concentrations. The new REA will also reflect the new information and model improvements now available including:

- A SO_2 air monitoring dataset that is greatly expanded with regard to both the number of monitoring locations for which hourly maximum 5-minute concentrations are available and the number for which all 5-minute values for each hour are available;
- Improvements in the air quality dispersion model, AERMOD, intended to reduce uncertainties in 1-hour concentration estimates;
- Greatly expanded database of activity diaries, providing a stronger foundation for population exposure modeling;
- Improvements to several aspects of APEX; and,
- Use of an expanded dataset for development of a lung function exposure-response function, addressing uncertainty in the shape of the response function across the range of the study data.

The results from a new REA are expected to provide an improved characterization of exposure and risk to inform EPA's review of the primary SO_2 standard.

Plans for the exposure-based risk assessment include assessment of recent air quality conditions and conditions just meeting the current standard in several study areas.[1] The study areas will be selected based on consideration of the magnitude of current SO_2 concentrations, number of monitors in the area, including those with 5-minute monitoring data, and population size. The risk characterization will be based on both comparisons of population 5-minute exposures at elevated ventilation to health-based benchmark levels and estimated population risk of "moderate" or greater SO_2-related lung function decrements. The analyses and results will be documented in a REA. Key findings of the REA will then be considered in the broader context of the Policy Assessment, which will also consider the current evidence as assessed in the ISA and characterization of SO_2 concentrations in ambient air across the U.S. based on recent monitoring data, with particular attention to peak 5-minute concentrations. The Policy Assessment provides staff analysis and conclusions regarding policy implications of the full array of currently available information in each NAAQS review for consideration by the Administrator.

[1] The need for additional air quality scenarios will be considered in the draft Policy Assessment that will accompany the draft REA presenting results for the analyses described in this REA Planning Document.

1 INTRODUCTION

The U.S. Environmental Protection Agency (EPA) is conducting a review of the air quality criteria and the primary (health-based)[2] national ambient air quality standard (NAAQS) for sulfur oxides (SO_X). The purpose of this planning document (titled *Review of the Primary National Ambient Air Quality Standard for Sulfur Oxides: Risk and Exposure Assessment Planning Document* – hereafter referred to as *REA Planning Document*) is to describe the consideration of the extent to which newly available scientific evidence, tools or methodologies, or information warrant the conduct of a quantitative risk and exposure assessment (REA) that might inform this review. Also considered is the extent to which newly available evidence may refine our[3] characterization of exposure and risk estimates provided by the assessments conducted for the last review. Based on these considerations, and as described below, we plan to develop a new REA to inform the current review of the primary NAAQS for SO_X. Accordingly, this document's additional purpose is to describe the general plan, including scope and methods for conducting the REA.

In the last review, while the EPA made a number of revisions to the standards, it also affirmed sulfur dioxide (SO_2) as the indicator for the NAAQS for SOx based on its more common occurrence in the atmosphere and the predominance of SO_2 studies in the health effects information for SOx (34 FR 1988, February 11, 1969; 75 FR 35520, June 22, 2010). The EPA also promulgated a new 1-hour standard to afford the requisite protection for at-risk populations such as people with asthma against an array of adverse respiratory health effects related to short-term SO_2 exposures. The 1-hour standard was set at a level of 75 parts per billion (ppb), based on the 3-year average of the annual 99th percentile of 1-hour daily maximum SO_2 concentrations. The EPA also revoked the then-existing 24-hour and annual primary standards based largely on the conclusion that the 1-hour standard would also control longer-term average concentrations, maintaining 24-hour and annual concentrations generally well below the levels of those standards, and on the lack of evidence indicating the need for such longer-term standards.

In conjunction with the revisions to the standards, the EPA required that monitoring agencies report 5-minute SO_2 measurements, either the highest 5-minute concentration for each hour of the day or all twelve 5-minute concentrations for each hour of the day. The rationale for

[2] The EPA is separately reviewing the welfare effects associated with sulfur oxides and the public welfare protection provided by the secondary SO_2 standard, in conjunction with a review of the secondary standards for nitrogen oxides and PM with respect to their protection of the public welfare from adverse effects related to ecological effects (U.S. EPA, 2017).

[3] In this document, the terms "staff," "we" and "our" refer to staff in the EPA's Office of Air Quality Planning and Standards (OAQPS).

this requirement was to provide additional monitoring data for use in subsequent reviews of the primary standard, particularly in considering the extent of protection provided by the 1-hour standard against 5-minute peak SO_2 concentrations of concern (75 FR 35554, June 22, 2010). These measurements are among the information newly available in this review that is considered in this document.

This document presents a critical evaluation of information related to SO_2 human exposure and risk newly available in the second draft of the *Integrated Science Assessment for Sulfur Oxides – Health Criteria* (U.S. EPA, 2016; hereafter referred to as second draft ISA). Advances in modeling tools and techniques and air quality data that have become available since the last review are also considered. This document is intended to facilitate consultation with the Clean Air Scientific Advisory Committee (CASAC), as well as an opportunity for public participation, on this evaluation of the potential support in the current information for updated quantitative analyses of SO_2 exposures and/or health risks, and on the plan for such analyses, as warranted. This evaluation has considered the degree to which newly available scientific evidence, tools or methodologies, or information may address or improve our consideration of important uncertainties associated with the analyses from the last review (summarized in chapter 2). Based on these considerations and our preliminary conclusions on the extent to which updated quantitative analyses of exposures and/or health risks are warranted in the current review (chapter 3), this document presents general plans for such analyses (chapter 4).

1.1 BACKGROUND

Sections 108 and 109 of the Clean Air Act (CAA) govern the establishment and periodic review of the NAAQS. Section 108 [42 U.S.C. 7408] directs the Administrator to identify and list certain air pollutants and then to issue air quality criteria for those pollutants. The Administrator is to list those air pollutants that in his "judgment, cause or contribute to air pollution which may reasonably be anticipated to endanger public health or welfare," "the presence of which in the ambient air results from numerous or diverse mobile or stationary sources;" and "for which…[the Administrator] plans to issue air quality criteria…" CAA section 108(a)(1). The NAAQS are established for these pollutants. The CAA requires that NAAQS are to be based on air quality criteria, which are intended to "accurately reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare that may be expected from the presence of [the] pollutant in the ambient air…" CAA section 108(a)(2). Under CAA section 109 [42 U.S.C. 7409], the EPA Administrator is to propose, promulgate, and periodically review, at five-year intervals, "primary" (health-based)

and "secondary" (welfare-based)[4] NAAQS for such pollutants for which air quality criteria are issued.[5] Based on periodic reviews of the air quality criteria and standards, the Administrator is to make revisions in the criteria and standards, and promulgate any new standards, as may be appropriate. The CAA also requires that an independent scientific review committee review the air quality criteria and standards and recommend to the Administrator any new standards and revisions of existing air quality criteria and standards as may be appropriate, a function now performed by the CASAC.

The overall plan for this review was presented in the *Integrated Review Plan for the Primary National Ambient Air Quality Standard for Sulfur Dioxide* (U.S. EPA, 2014, hereafter referred to as IRP). That plan discusses the preparation of key documents in the NAAQS review process including an Integrated Science Assessment (ISA), a Risk and Exposure Assessment (REA; as warranted), and a Policy Assessment (PA). In general terms, the ISA is to provide a critical assessment of the latest available scientific information upon which the NAAQS are to be based, and the Policy Assessment is to evaluate the policy implications of the information contained in the ISA and of any policy-relevant quantitative analyses, such as a quantitative REA, that were performed for the review or for past reviews. Based on that evaluation, the Policy Assessment presents staff conclusions regarding standard-setting options for the Administrator to consider in reaching decisions on the NAAQS.[6]

1.2 CONCEPTUAL MODEL FOR SO_2 EXPOSURE AND RISK

This section describes the conceptual model for exposure and associated health risk of SO_2 in ambient air. The model summarizes our consideration of the currently available information on emissions sources, exposure pathways, routes of exposure, exposed populations, health endpoints and risk metrics. This general model, illustrated in Figure 1-1, guided our

[4] Section 302(h) of the CAA provides that all language referring to effects on welfare includes but is 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…"

[5] Section 109(b)(1) [42 U.S.C. 7409] of the CAA defines a primary standard as one "the attainment and maintenance of which in the judgment of the Administrator, based on such criteria and allowing an adequate margin of safety, are requisite to protect the public health." Section 109(b)(2) of the CAA directs that a secondary standard is to "specify a level of air quality the attainment and maintenance of which, in the judgment of the Administrator, based on such criteria, is requisite to protect the public welfare from any known or anticipated adverse effects associated with the presence of [the] pollutant in the ambient air."

[6] Review of NAAQS involve consideration of the four basic elements of a standard: indicator, averaging time, form, and level. The indicator defines the pollutant to be measured in the ambient air for the purpose of determining compliance with the standard. The averaging time defines the time period over which air quality measurements are to be obtained and averaged or cumulated. The form of a standard defines the air quality statistic that is to be compared to the level of the standard in determining whether an area attains the standard. The level of a standard defines the air quality concentration used (i.e., an ambient air concentration of the indicator pollutant).

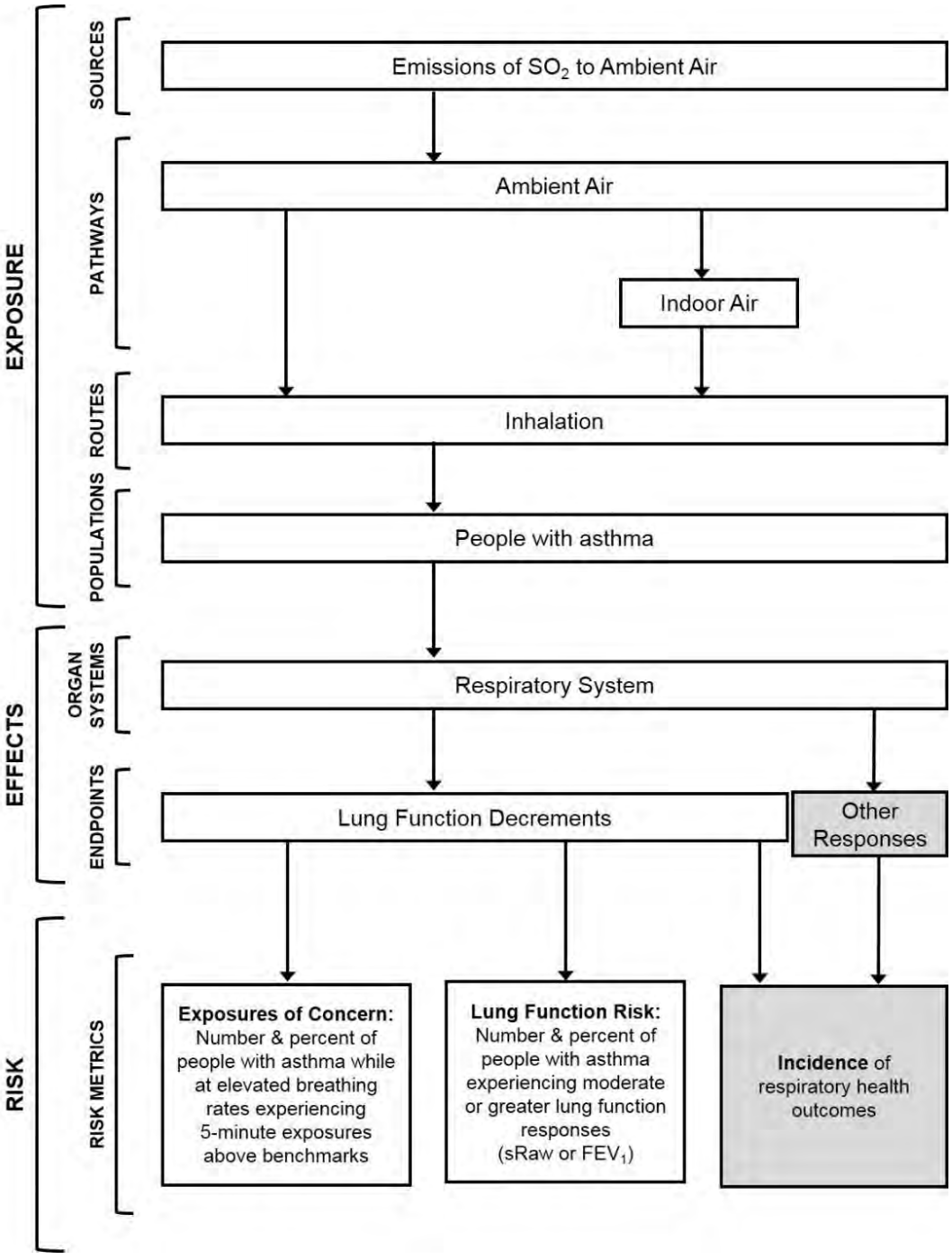
assessment in the last review and, as discussed in section 3.5 below, it remains appropriate in the current review.

Exposure pathways relevant for SO_2 are impacted by emissions sources, chemistry, meteorology, and ambient air concentrations. Anthropogenic SO_2 emissions originate primarily from point sources, including coal-fired electricity generating units (EGUs) and other industrial facilities (U.S. EPA 2008 [hereafter referred to as the 2008 ISA], section 2.1; second draft ISA, section 2.2.1). The point source nature of these emissions contribute to the relatively high spatial variability of SO_2 concentrations (both ambient air and exposure) compared with pollutants such as particulate matter (PM) and ozone (O_3) (second draft ISA, section 3.2.3). Another contributing factor to spatial variability is the dispersion and oxidation of SO_2 in the atmosphere, resulting in decreasing SO_2 concentrations with increasing distance from the source. SO_2 travels as a plume which may or may not impact large portions of surrounding populated areas depending on meteorological conditions. Concentrations of SO_2 in ambient air do not exhibit consistently strong temporal variability over daily or seasonal time scales, although in some areas concentrations are low during nighttime and show a daytime maximum, impacting temporal exposure patterns (2008 ISA, Figure 2-24; second draft ISA, Figures 2-26 and 2-27). The largest natural sources of SO_2 are volcanoes and wildfires. Indoor SO_2 sources can include secondary heating sources (e.g., fireplaces, space heaters), however, personal SO_2 exposure measurements have generally been lower than ambient air concentrations, indicating personal exposure to generally be dominated by ambient air exposure (2008 ISA, section 2.6.3; second draft ISA, section 3.4.1). The information newly available in this review supports, and in some cases augments with more detail (e.g., more extensive ambient monitoring information), these aspects our conceptual model.

Regarding exposed populations and health endpoints, the 2009 REA focused on lung function decrements in people with asthma while at moderate or greater exertion. This reflected the 2008 ISA conclusion there was sufficient evidence to infer a causal relationship between respiratory morbidity and short-term (5-minutes to 24-hours) exposure to SO_2. Key supporting evidence came from controlled human exposure studies that showed lung function decrements (as measured by reductions in forced expiratory volume, FEV_1, and increased specific airway resistance, sRaw) and respiratory symptoms in adult individuals with asthma exposed to SO_2 for 5-10 minutes while at elevated breathing rates (2008 ISA, section 5.2; second draft ISA, section 5.2).[7] As discussed in section 3.2, the information available in this review continues to support these primary health effects conclusions and their inclusions in the conceptual model.

[7] These aspects of the health effects evidence and its use in the 2009 REA are summarized in section 2.2.3.

In the last review, risks of these health effects to this at-risk population were characterized through two types of metrics. The first was characterization of the extent to which individuals with asthma were estimated to experience 5-minute exposures at or above concentrations of potential concern (based on benchmark levels described in section 2.2.3) while they were at elevated breathing rates. The assessment also characterized the extent to which individuals with asthma were estimated to experience moderate or greater lung function responses (as measured by FEV_1 or sRaw) as a result of 5-minute SO_2 exposures while at elevated breathing rates. As discussed in chapters 3 and 4, these types of risk metrics are also considered for the current review.



Note: The grey boxes indicate elements not included.

Figure 1-1. Conceptual model for exposure and associated health risk of SO_2 in ambient air.

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2 OVERVIEW OF THE PREVIOUS ASSESSMENT

This chapter summarizes the assessment in the last review, which is described in more detail in the *Risk and Exposure Assessment to Support the Review of the SO_2 Primary National Ambient Air Quality Standards: Final Report* from the last review (U.S. EPA 2009; hereafter referred to as 2009 REA). This chapter begins with an overview of the analysis approach and modeling elements in the last review (section 2.1). The overview section also describes, for the last review, the analyses of monitoring data (section 2.1.1), air quality scenarios (section 2.1.2), the health endpoint, concentration-response, and risk metrics (section 2.1.3), and the relationship used to estimate 5-minute concentrations from 1-hour SO_2 concentrations (section 2.1.4). Section 2.2 describes the air quality-based assessment and section 2.3 describes the risk and exposure assessment for the last review, as well as the key uncertainties and limitations.

2.1 ANALYSIS APPROACH AND MODELING ELEMENTS

In each NAAQS review, selection of the approach most appropriate for the characterization of risks is influenced by the nature and strength of the evidence for the subject pollutant. Depending on the type of evidence available, analyses may include quantitative risk assessments based on dose-response, exposure-response, or ambient air concentration-response relationships. Analyses may also be based on comparisons of exposure estimates or ambient air quality concentrations (i.e., as surrogates for potential ambient air exposures) with concentrations of potential concern, based on findings of controlled human exposure studies. This section summarizes the assessment approach (including discussion of key analysis steps) used in the last review. As illustrated in Figure 2-1, the REA completed for the 2010 review employed two health risk approaches, one based on ambient air concentrations alone and the second incorporating estimates of human exposure. Both approaches evaluated potential health risk using several different air quality scenarios, including a scenario that considered unadjusted ambient air concentrations ("as is" air quality) as well as scenarios that considered ambient air concentrations adjusted to just meet the then-existing and several potential alternative standards (see section 2.1.2 for details).

In the first assessment approach, SO_2 concentrations at ambient air monitors were used as a surrogate for exposure in 40 U.S. counties. This air quality-based assessment evaluated the number of days (per monitor and per year) that daily 5-minute maximum SO_2 concentrations in ambient air exceeded the 5-minute concentrations of potential concern (referred to as "benchmark levels"). Section 2.1.1 provides a brief summary of air quality analyses of the larger set of ambient air monitoring data across the U.S. for the years 1997 through 2007. The air

quality-based assessment approach and the associated key uncertainties and limitations are described in section 2.2.

In the exposure-based approach, risk was characterized two ways. For both, population-based estimates of human exposure were developed using an exposure model in order to account for time people spend in different microenvironments, as well as for time spent at elevated ventilation rates while exposed to peak 5-minute SO_2 concentrations. The model simulated populations in two study areas: Greene County, MO and a three-county portion of the St. Louis Metropolitan Statistical Area (MSA). The populations simulated included all people with asthma, with results also presented particular to the subset of those that were children. Health risk was characterized in the following ways:

- *Exposures Above Benchmarks:* The 5-minute exposure concentrations of individuals at elevated ventilation rates within each study area were compared to 5-minute benchmark levels. The number and percent of people with asthma exposed, while at elevated ventilation, to 5-minute daily maximum SO_2 concentrations that exceeded the benchmark levels were estimated for each air quality scenario.
- *Lung Function Risk:* Lung function risk was estimated by combining the population-based 5-minute exposure estimates with two exposure-response (E-R) functions, also derived from the controlled human exposure studies. Results were reported in terms of the number and percent of exposed people with asthma estimated to experience moderate or greater lung function responses (in terms of FEV_1 and sRaw) at least once per year and the total number of such lung function responses estimated to occur per year.

Details for these two health risk and exposure assessment approaches and the key associated uncertainties and limitations are described in section 2.3.

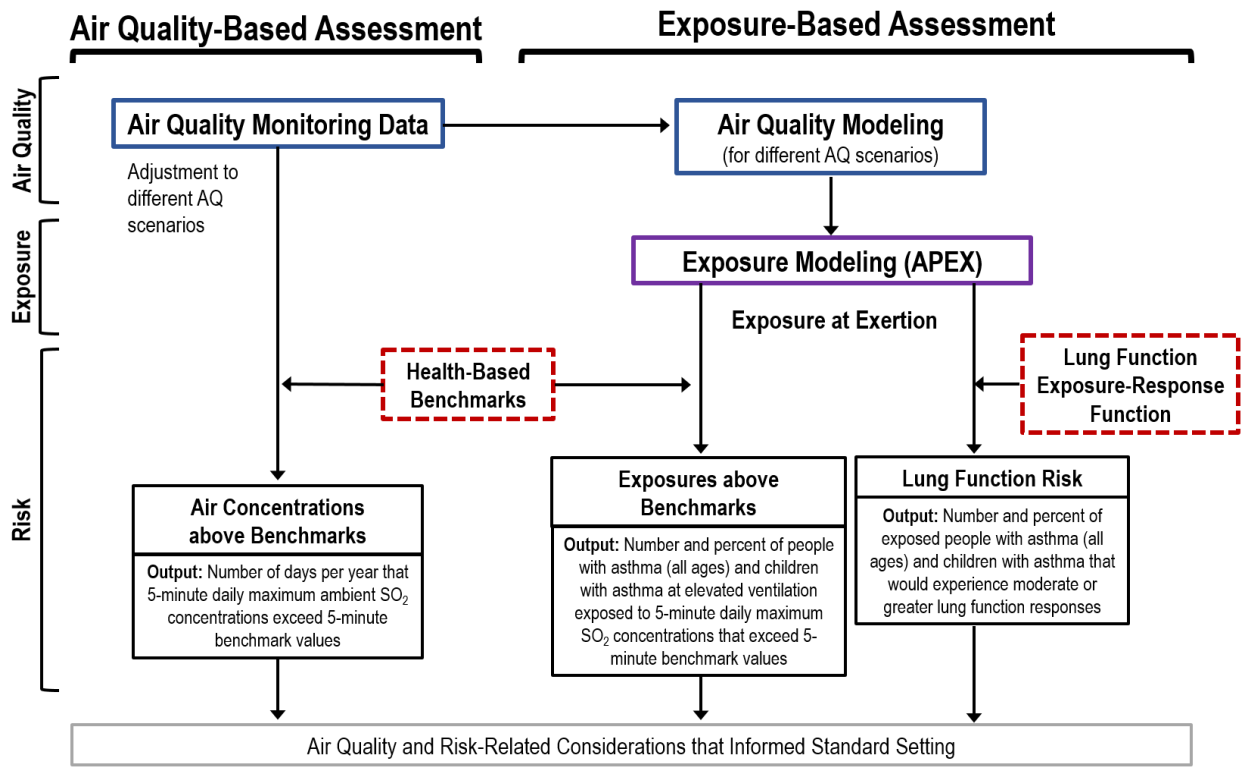

Figure 2-1. Overview of analysis approach for 2009 REA. Blue boxes indicate approach for estimating air concentrations, purple boxes indicate exposure modeling, and red dashed boxes indicate use of health effects information.

2.1.1 Additional Analyses of Monitoring Data

Unadjusted (*as is*) air quality data from 1997 through 2007 were analyzed with regard to relationships between annual average, 24-hour average, and daily maximum 1-hour concentrations and 5-minute concentrations. The analyses were conducted with two sets of data: (1) a dataset of 98 locations where both the 1-hour and 5-minute maximum SO_2 concentrations were reported and (2) a dataset of 809 locations at which measured 5-minute SO_2 concentrations were not available but were estimated using available 1-hour SO_2 concentrations and a statistical model described in section 2.1.4 below (2009 REA, sections 7.3.1 and 7.3.2). Other analyses estimated the probabilities of 5-minute concentrations above benchmarks of interest for different 24-hour or 1-hour average concentrations. The results of these analyses were among the considerations contributing to the EPA's selection of a 1-hour averaging time for the new standard promulgated in 2010 to address exposures as short as 5 minutes (75 FR 35539, June 22, 2010).

2.1.2 Air Quality Scenarios

The air quality scenarios evaluated were for *as is* air quality, air quality adjusted to just meet the then-existing standards, and air quality adjusted to just meet potential alternative 1-hour

daily maximum standards, as listed in Table 2-1. Just meeting the then-existing NAAQS meant adjusting concentrations to just meet either a 30 ppb annual average or the 140 ppb 24-hour average concentration (one allowed exceedance) at the highest monitor in a study area, whichever was the controlling standard at that ambient air monitor (2009 REA, section 7.2.4). The potential alternative 1-hour standards were evaluated using two percentile forms, the 98th and 99th percentile. These forms were chosen as options that provided an appropriate balance between limiting the occurrence of peak concentrations and providing a stable and robust regulatory target (2009 REA, section 5.4).

Table 2-1. Air quality scenarios evaluated in the 2009 REA.

Air Quality Scenarios		
"As is" conditions	Unadjusted air quality	
Current (then-existing) Standards	140 ppb, 24-hour average, no more than one exceedance in a year	
	30 ppb, annual average not to be exceeded	
Potential Alternative 1-hour Standards	3-year average of 98th percentile daily maximum 1-hour =	100 ppb[a]
		200 ppb
	3-year average of 99th percentile daily maximum 1-hour =	50 ppb
		100 ppb
		150 ppb
		200 ppb
		250 ppb

[a] This level was not evaluated for this form in the exposure-based assessment.

2.1.3 Benchmark Levels, Exposure-Response, and Risk Metrics

The 2009 REA focused on the health endpoint identified by the 2008 ISA as being causally related to SO_2 exposures (i.e., respiratory effects), and more specifically, decrements in lung function in individuals with asthma at elevated exertion levels. This evidence comes largely from controlled human exposure studies that demonstrated a relationship between 5- and 10-minute peak SO_2 exposures in exercising individuals with asthma and decrements in lung function that are frequently accompanied by respiratory symptoms. Lung function decrements were quantified by reductions in forced expiratory volume, FEV_1, and increased specific airway resistance, sRaw. The studies demonstrated that individuals with asthma exposed to SO_2 concentrations as low as 200-300 ppb for 5-10 minutes during exercise experienced moderate or greater bronchoconstriction, measured as a decrease in FEV_1 of $\geq$ 15% or an increase in sRaw of $\geq$ 100% (2008 ISA, section 3.1.3.2).

Among individuals with asthma, the 2008 ISA found that both the percent of individuals affected and the severity of response increased with increasing SO_2 concentrations across the range studied. At concentrations ranging from 200-300 ppb, the lowest levels tested in free breathing chamber studies,[8] 5-30% of exercising individuals with asthma experienced moderate or greater decrements in lung function (2008 ISA, Table 3-1). At concentrations ≥ 400 ppb, moderate or greater decrements in lung function occurred in 20-60% of exercising individuals with asthma and a larger percentage of individuals with asthma experienced severe decrements in lung function (i.e., ≥ 200% increase in sRaw, and/or ≥ 20% decrease in FEV_1), compared to exposures at 200-300 ppb (2008 ISA, Table 3-1). Additionally, at concentrations ≥ 400 ppb, moderate or greater decrements in lung function were frequently accompanied by respiratory symptoms (2008 ISA, Table 3-1).

These controlled human exposure study data were used in two ways: (1) to identify exposure concentrations of potential concern (benchmark levels) and (2) to derive E-R functions for lung function decrements. The benchmark levels were compared to SO_2 air concentrations and modeled estimates of human exposure (section 2.3.3 below) to characterize potential health risks. The E-R functions were combined with outputs from the exposure modeling to quantitatively estimate lung function risk for exposed individuals with asthma (section 2.3.4 below). The identification of potential health effect benchmarks and the derivation of the E-R functions are briefly described below and more detailed information can be found in the 2009 REA.

The benchmark levels are concentrations chosen to represent "exposures of potential concern" which were used in the analyses to estimate exposures and risks associated with 5-minute concentrations of SO_2 (75 FR 35527, June 22, 2010). Based on the evidence in the 2008 ISA and recommendations from the CASAC, staff concluded that it was appropriate to examine 5-minute benchmark levels in the range of 100-400 ppb (2009 REA, chapter 7). The comparisons of SO_2 concentrations to benchmark levels provided perspective on the extent to which, under various air quality scenarios, there was the potential for at-risk populations to experience SO_2 exposures that could be of concern.

[8] In addition to "free-breathing" studies (i.e., studies in which individuals breathe the air while sequestered in a large chamber), a limited number of studies assessed effects based on exposures delivered via mouthpiece breathing. A few of these studies assessed exposure concentrations as low as 100 ppb (e.g., Sheppard et al. 1981 exposed two subjects to 100 ppb SO_2), although some methodological aspects of the studies limit the conclusions the ISA has drawn from them. Further, such studies that utilize a mouthpiece exposure system cannot be directly compared to studies involving freely breathing subjects, as nasal absorption of SO_2 is bypassed during oral breathing, thus allowing a greater fraction of inhaled SO_2 to reach the tracheobronchial airways. As a result, individuals exposed to SO_2 through a mouthpiece are likely to experience greater respiratory effects from a given SO_2 exposure (second draft ISA, p. 5-22).

The exposure-based risk assessment also included two types of lung function responses (i.e., sRaw and FEV_1) and two levels of response (≥ 100% and 200% increase for sRaw and ≥ 15% and 20% decrease for FEV_1). The risk estimates were based on using two different functional forms for the E-R function: a 2-parameter logistic model and a probit model.[9] Risk estimates based on sRaw as the measure of lung function response were given primary emphasis in the 2009 REA because the E-R relationships were developed using a greater number of samples collected from individual subjects, which provided more confidence in the E-R relationship when compared with that developed for the FEV_1 health endpoint.[10] Lung function risk estimates were presented as a range based on using the two model forms. Risk was estimated across the full range of estimated exposures, including exposure concentrations below those assessed in the controlled human exposure studies (2009 REA, section 9.2.3).

2.1.4 Relationship Between 1-Hour and 5-Minute Concentrations

Based on the health effects information summarized above, the 2009 REA focused on exposures and risk associated with 5-minute concentrations of SO_2. While a majority of the then-existing SO_2 monitoring network sites reported 1-hour average SO_2 concentrations, only a limited number of ambient air monitors reported 5-minute maximum SO_2 concentrations. A statistical model was developed to extend the 5-minute SO_2 air quality characterization to locations where 1-hour average SO_2 concentrations were reported and associated 5-minute concentrations were not.

Peak-to-mean ratios (PMRs) were obtained by dividing the 5-minute maximum SO_2 concentration occurring within an hour by the corresponding 1-hour SO_2 concentration. Distributions of PMRs were generated using 1-hour concentrations and categorical variables in defining the distributions of PMRs. Using probabilistic sampling and this statistical relationship, every 1-hour concentrations of SO_2 at ambient air monitors and at air quality-modeled receptor locations was assigned a 5-minute maximum SO_2 concentration. More information about the development and evaluation of PMRs is described in section 7.2.3 of the 2009 REA.

2.2 AIR QUALITY-BASED ASSESSMENT

In the air quality-based assessment of the then-existing and potential alternative standards, adjusted ambient air monitoring data were used as an indicator of potential human

[9] A distribution of E-R relationships was developed using a probabilistic Bayesian Markov Chain Monte Carlo sampling approach for the pooled dataset of all study participant responses (i.e., individual-level vs study level-responses). The 2009 REA focused on use of the median logistic and probit E-R functions from the generated distribution of E-R functions (2009 REA, Appendix C, section 3.2).

[10] Risk estimates using FEV_1 as the indicator of lung function response are available in the 2009 REA in Tables 4-3, 4-4, 4-7, and 4-8 in Appendix C.

exposure. Focusing on monitoring locations in 40 county-based study areas, 5-minute concentrations estimated to occur in these air quality scenarios were compared to the benchmark levels to provide a characterization of the potential for exposures of concern. Section 2.2.1 below describes estimation of 1-hour and 5-minute concentrations in these scenarios, using the air quality adjustment approach and model for estimating 5-minute concentrations mentioned above in sections 2.1.2 and 2.1.4, respectively. Selection of the 40 counties for the analysis is described in section 2.2.2. The benchmark comparison analysis and uncertainties and limitations associated with this assessment approach are summarized in sections 2.3.3 and 2.3.5, respectively.

2.2.1 Air Concentrations

The air quality scenarios evaluated in the assessment and mentioned in section 2.1.2 above, included the measured SO_2 concentrations, *as is*, and the ambient air concentrations adjusted to reflect air quality conditions just meeting the then-existing and potential alternative standards. Taking into consideration policy-relevant background (PRB) concentrations[11] and how the distribution of ambient air concentrations of SO_2 had changed over time,[12] a proportional approach was used when adjusting ambient air concentrations to just meet a particular existing or potential alternative standard. The adjustment for each scenario is summarized in Table 2-2 below and described in more detail in section 7.2.4.1 of the 2009 REA.

In adjusting ambient air concentrations to just meet the then-existing standards, the highest monitor (in terms of concentration) within a county was adjusted so that it just met either the 24-hour or annual standard, whichever was the controlling standard. As a result of the rounding conventions and the forms for these standards, operationally this meant that the highest monitor (in terms of concentration) within a county was adjusted so that it just met either a 144 ppb 24-hour average (2nd highest) or 30.4 ppb annual average, whichever was the controlling standard.[13]

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[11] PRB was determined to be well below concentrations that might cause potential health effects and constituted a small percent (<1%) of the SO_2 concentrations in ambient air at most locations and was not considered separately in characterizations of health risks associated with the air quality scenarios (2009 REA, section 2.3). In monitoring locations where PRB was expected to be of particular importance (e.g., Hawaii County, HI), data were noted as being influenced by significant natural sources (e.g., volcanoes) rather than anthropogenic sources and were not used in any of the air quality analyses.

[12] While annual average concentrations of SO_2 had declined significantly since the late 1970s, variability in both 5-minute and 1-hour concentrations remained relatively constant when considering the collective air quality data or at an individual monitor. The relationship between percentile values of the distribution of daily maximum 1-hour SO_2 concentrations during a low and a high year was generally linear. More details on these analyses are available in section 7.2.4.1 of the 2009 REA.

[13] By definition, the controlling standard was the standard that allowed air quality to just meet either the 2nd highest 24-hour concentration level of 144 ppb (i.e., the 24-hour standard was the controlling standard) or the annual concentration level of 30.4 ppb (i.e., the annual standard was the controlling standard). The adjustment factor was

For the air quality scenarios representing the potential alternative standards, proportional adjustment factors were derived considering their respective forms, averaging times, and levels. The 98th and 99th percentile 1-hour daily maximum SO_2 concentrations averaged across three years of monitoring were used to calculate proportional adjustment factors at five potential alternative standard levels: 50, 100, 150, 200, and 250 ppb. The 1-hour concentrations at the monitor with the highest 1-hour concentration, in terms of the 3-year average at the 98th or 99th percentile, were adjusted such that they just met the particular 1-hour alternative standard. All other monitor concentrations in that county were adjusted using the same factor, resulting in concentrations at those monitors below that of the selected 1-hour alternative standard.

Table 2-2. Adjustment approach for each air quality scenario in the 2009 REA.

<table>
<tr><th colspan="2">Air Quality Scenario</th><th>Approach to represent air quality just meeting different standards</th></tr>
<tr><td>As is</td><td>n/a</td><td>- No adjustment</td></tr>
<tr><td rowspan="2">Current (then-existing) Standard</td><td>140 ppb, 24-hour average, no more than one exceedance in a year</td><td rowspan="2">Within each study area, a proportional adjustment factor was derived (for each of the years from 2001 to 2006) from the level of the controlling standard (whichever yielded the smaller adjustment factor):
- The factor was derived as the level for the controlling standard divided by the maximum concentration at a location in terms of the controlling standard (for each year)
All hourly SO_2 concentrations in a study area for each year were then multiplied by same adjustment factor (for that year).</td></tr>
<tr><td>30 ppb, annual average not to be exceeded</td></tr>
<tr><td>Potential Alternative Standard</td><td>Multiple levels in terms of 3-year average of 98th percentile (or 99th percentile) daily maximum 1-hour in each year</td><td>Within each study area, a proportional adjustment factor was derived considering the form, averaging time, and levels of potential alternative standards
- The factor was derived as the level for the potential alternative standard divided by the maximum concentration at a location in terms of that potential alternative standard, for each of the two 3-year periods (2001-2003 and 2004-2006)
All hourly SO_2 concentrations in a study area for a given 3-year period were multiplied by same adjustment factor.</td></tr>
</table>

derived from a single monitor within each county for a given year, even if there was more than one monitor in the county. A different (or the same) monitor in each county could have been used to derive the adjustment factor for other years. The only requirement for selection was that it was the lowest adjustment factor, whether it was derived from the annual or 24-hour standard level.

The maximum 5-minute SO_2 concentration was estimated for each adjusted 1-hour measurement in each air quality scenario based on the statistical model described in section 2.2.4. Because statistical distributions of PMRs were developed, the maximum 5-minute concentration was approximated by averaging 20 individual model simulations for each 1-hour concentration. Then the estimated maximum 5-minute concentrations for each hour at each monitor were used to generate the health risk metric of interest (e.g., the number of days per year with a 5-minute benchmark level exceedance).

2.2.2 Study Areas and Years

To maintain a computationally manageable dataset given the number of air quality scenarios (nine) and benchmark levels (four), the air quality-based analysis of existing and potential alternative standards was focused on 40 county-based study areas and the most recent years for which complete data were available (2001-2006). The counties were selected based on two criteria: occurrence of elevated 5-minute SO_2 concentrations and how close air quality conditions were to just meeting the then-existing annual and 24-hour standards (and having data from at least two monitors within a county). Based on the first criterion, two counties in Missouri, where the monitors with the most frequently measured number of daily 5-minute maximum SO_2 concentrations at or above the benchmark levels were located, were included.[14] An additional 38 counties/study areas were included based on the second criterion and having at least two monitors.[15] This second criterion minimized the adjustment required to reflect air quality just meeting the then-existing standards. More information about the selection criteria and locations is provided in the 2009 REA (2009 REA, section 7.2.4.2 and Table 7-7).

2.2.3 Comparison of Air Concentrations to Benchmarks

For each air quality scenario, daily maximum 5-minute concentrations at monitor locations in the 40 counties were compared to the 5-minute benchmark levels. The results of these comparisons were summarized using several metrics: (a) the probability of daily 5-minute maximum SO_2 concentrations above each of the benchmark levels, and (b) number of days per year with a maximum 5-minute concentration above each of the benchmark levels. In considering these results in the last review with regard to adequacy of the then-existing standard and the appropriateness of potential alternative standards, the Administrator gave particular

[14] For more information on the number and frequency of measured 5-minute SO_2 concentrations that exceeded benchmark levels, see section 7.2.4.2 and table A.5-1 in Appendix A.5 of the 2009 REA.

[15] Adjustment factors were derived for each county and year for those counties having at least two monitors operating in the county for five of the six possible monitoring years. The counties were then ranked in ascending order based on the adjustment factor and the top 38 values were selected. These additional 38 counties all had at least two monitors and the lowest adjustment factors (2009 REA, section 7.2.4.2).

attention to the benchmark levels of 200 and 400 ppb based on several considerations including judgments related to adversity (75 FR 35520, June 22, 2010).

2.2.4 Key Uncertainties and Limitations

The aspects of the air quality-based assessment contributing to uncertainty in the results are summarized here. Some of these uncertainties are also discussed in Chapter 3, in the context of considering information newly available in this review and the extent to which its use would be likely to substantially address such uncertainties.

The air quality-based assessment performed in the last review was considered to provide a broad characterization of national air quality and what it might indicate with regard to human exposures that might be associated with 5-minute SO_2 concentrations. An advantage of the air quality-based assessment was the relative simplicity of the approach. However, there are uncertainties associated with the assumption that SO_2 concentrations in ambient air can serve as an adequate surrogate for total exposure to SO_2 from ambient air. Such uncertainties are summarized below.

- *Ambient air concentrations as a surrogate of exposures to at-risk populations while at elevated exertion:* Actual exposures may be influenced by factors not considered by the air quality-based assessment approach, including small-scale spatial variability in SO_2 concentrations in ambient air (which might not have been represented by the ambient air monitoring network) and spatial/temporal variability in human activity patterns. This type of approach does not include these influential factors that affect microenvironmental concentrations and the frequenting and time spent in different geographic areas and thus, the extent to which at-risk individuals are exposed (75 FR 35528, June 22, 2010). This approach also does not account for breathing rates of potentially exposed individuals, which is important for SO_2 as the exposures of concern are those incurred while at elevated ventilation rates.
- *Concentrations of SO_2 in ambient air as an indicator of SO_2 exposure:* The strength of the relationship between SO_2 concentrations in personal air and ambient air is supported by the limited presence of indoor sources of SO_2, indicating that much of an individual's personal exposure is from ambient air exposures. However, ambient air monitored SO_2 concentrations are typically much higher than that of a personal exposure concentration, in part because SO_2 is consumed by reactions on indoor surfaces (2008 ISA, section 2.6.3). Therefore, while the relationship between personal exposures and ambient air concentrations is strong, the use of monitoring data as an indicator of SO_2 exposure may lead to an overestimation of exposure concentrations and of the number of exposure concentrations of concern that individuals may encounter. The knowledge-base uncertainty for this area was characterized as high (2009 REA, Table 7-16).
- *Development of benchmark levels:* This area is summarized in section 2.3.4 below.
- *Selection of 5-minute averaging time for concentrations to compare to benchmark levels:* The SO_2 exposure durations in the controlled human exposure studies were generally between 5 and 10 minutes. The evidence indicates that onset of symptoms occurs within

minutes in response to the study exposure concentrations, indicating responsiveness to the "peak" concentration encountered (2008 ISA, section 3.1; U.S. EPA, 1994, section 4.1). Further, there was general consistency in the observed responses for 5-minute and 10-minute exposures to the same concentration.

- *Single count of exceedances versus multiple exceedances per day:* This approach reported the observed or estimated number of days that the maximum 5-minute SO_2 concentration exceeded a particular benchmark level. Although there could be multiple exceedances of the benchmark levels in a day, none of the elements of exposure were considered (e.g., whether or not time of exposure occurred coincident with elevated activity level) in the air quality-based assessment, thus limiting the relevance of multiple exceedances within a day.

Data for SO_2 from both the limited number of monitors reporting 5-minute concentrations and the broader network of monitors reporting 1-hour concentrations of SO_2 were used to characterize air quality. A number of uncertainties were identified related to the SO_2 monitoring data and monitoring network and are briefly described below.

- *Database quality for air quality data:* Concentrations of SO_2 reported in the Air Quality System (AQS) were assumed to be quality assured. To the extent there were poor quality data in AQS, retention of poor quality high concentration data would have had a greater impact on the estimated number of exceedances of benchmark levels than retention of poor quality low concentration data. However, given the number of ambient air measurements considered, staff concluded that even if there were a few poor quality high concentration data points, they would not have had a large impact on the REA results (2009 REA, section 7.4.2.1).

- *Ambient air measurement technique:* There is the potential for other compounds in ambient air (e.g., polycyclic aromatic hydrocarbons) to interfere with SO_2 ambient air measurements. The 2008 ISA identified several sources of positive and negative interference that could have increased the uncertainty in the measurement of SO_2 concentrations (2008 ISA, sections 2.3.1 and 2.3.2). However, many of the sources of interference were described to have limited impact due to instrument controls designed to prevent the interference (2009 REA, section 7.4.2.2).

- *Temporal representation of monitoring data:* The missing values in a given valid year of data may lead to uncertainty in the temporal representation of concentration distributions, considering both the 5-minute and 1-hour averages. In addition, the use of multiple years of historical air quality data may also contribute some uncertainty given long-term trends in ambient air monitoring and concentration variability. However, given the overall completeness of the monitoring data, that the range of concentration variability did not differ significantly across most monitoring years, and considering the focus in the 40-county analysis used a limited period (2001-2006), the impact of this factor is likely limited (2009 REA, section 7.4.2.3).

- *Spatial representation of monitoring network:* The spatial representativeness of the monitoring network may contribute uncertainty, particularly if the monitoring network is not dense enough to resolve the spatial variability in SO_2 concentrations and if the monitors are not effectively distributed to represent population exposures. The limited

number of monitors, particularly when considering those monitors that reported 5-minute maximum SO_2 concentrations, contributes to uncertainty (characterized as high for knowledge base) in this area (2009 REA, section 7.4.2.4).

- *Air quality adjustment procedure:* To derive the air quality conditions for each air quality scenario, the proportional adjustment factors derived from a study area's design value monitor were applied to adjust all ambient air monitors in the study area (2009 REA, section 7.4.2.5). This area is summarized in section 2.3.4 below.
- *Statistical model used for estimating 5-minute SO_2 concentrations:* A number of uncertainties were identified regarding the statistical model developed and used to estimate 5-minute concentrations and its impact on the number of benchmark level exceedances (2009 REA, section 7.4.2.6). This area is summarized in section 2.3.4 below.

2.3 RISK AND EXPOSURE ASSESSMENT

In the exposure-based assessment, a combined air quality and exposure modeling approach was used to generate estimates of 5-minute maximum SO_2 exposures for at-risk populations residing in two study areas: (1) Greene County, MO; and, (2) a three-county portion of the St. Louis MSA. In these two case study areas, census block-level hourly SO_2 concentrations in ambient air were estimated using AERMOD, a dispersion model, using emissions estimates from stationary, non-point, and port sources. The Air Pollutants Exposure (APEX) model, a human exposure model, was used to estimate 5-minute exposures for individuals in the simulated at-risk populations using the census block-level hourly SO_2 concentrations estimated by AERMOD and the relationship between 1-hour and 5-minute concentrations described in section 2.2.4 above.

For each air quality scenario, simulated individual exposure profiles were used to derive two types of risk metrics: (1) the number of days per year a simulated at-risk individual (at moderate or greater exertion) had at least one 5-minute exposure above the benchmark levels of 100, 200, 300, and 400 ppb and (2) the number and percent per year of simulated at-risk individuals that would experience moderate or greater lung function decrements in response to 5-minute daily maximum peak exposures while engaged in moderate or greater exertion (2009 REA, chapters 8 and 9).

2.3.1 Study Areas, Time Period, and Simulated Population

Overall, the study areas and time period for the assessment were selected based on availability of ambient air monitoring data, the presence of significant and diverse SO_2 emission sources, population demographics, and results of the air quality-based assessment (section 2.3). Staff focused on areas most likely to have elevated 5-minute SO_2 concentrations and having a sufficient number of ambient air measurements for the analysis. Further, appropriate

consideration of resources available and that were needed for this type of assessment (e.g., computational, time, funding) resulted in selection of two study areas.

Study areas in Missouri were investigated based on preliminary screening of the available 5-minute SO_2 monitoring data, which indicated the state of Missouri to be one of only a few states that reported both 5-minute maximum and continuous 5-minute SO_2 ambient air monitoring data at numerous (14) monitor locations. Missouri also had more than 30 monitors operating at some time during the period from 1997 to 2007 that measured 1-hour SO_2 concentrations. Additionally, exceedances above the benchmark levels were frequently observed at several of the 1-hour ambient air monitors within Missouri (e.g., Iron and Jefferson county monitors identified in Table 7-7 in the 2009 REA). The 2002 National Emissions Inventory (NEI) ranked Missouri 7th out of all U.S. states for the number of stacks with annual SO_2 emissions greater than 1000 tons. Stack emissions were associated with a number of source types, including electrical power generating units, chemical manufacturing, cement processing, and smelters.

Based on preliminary modeling, the availability of relevant ambient air monitoring data and baseline conditions (*as is* air quality), Greene County and three counties within the St. Louis MSA were selected as the two study areas. Greene County had a number of ambient air monitors and well-defined data for most model inputs (2009 REA, section 8.3.1). St. Louis is a large urban area with a combination of large emission sources and large potentially exposed populations (2009 REA, section 8.3.1). The year 2002 was simulated for both modeling domains to characterize the most recent year of emissions data available for the study areas.

The exposure assessment focused on simulated population groups that were considered more susceptible to potential health risks associated with SO_2 exposures as identified in the 2008 ISA; this included individuals (all ages) with asthma and a subset of that population, i.e., children with asthma. Based on the observed responses in the controlled human exposure studies, the focus for the exposure assessment was also centered on the maximum 5-minute exposures experienced by simulated individuals while at moderate or greater exertion levels during the exposure event (see section 2.1.3 above).

2.3.2 Exposure Modeling

Exposure models estimate human exposure taking into account pollutant concentrations in different locations visited and activities performed while occupying those locations. Different human activities, such as spending time outdoors, indoors, or driving, will result in varying pollutant exposure concentrations. The APEX model, developed by EPA for estimating human population exposure to criteria and toxic air pollutants, was used in this assessment to best

account for the dynamic nature of human exposure, considering important anthropometric, physiological, and physical factors that most influence exposures (2009 REA, section 8.2).

APEX is a probabilistic model designed to account for sources of variability that affect people's exposures. APEX simulates the movement of individuals through time and space and estimates their exposure to a given pollutant in indoor, outdoor, and in-vehicle microenvironments. The model stochastically generates simulated individuals using census-derived probability distributions for demographic characteristics based on the information from the Census at the tract, block-group, or block-level. In the 2009 REA, a national commuting database based on 2000 census data is also used to probabilistically estimate work commuting flows for those employed outside of their home. Any number of simulated individuals can be modeled, and collectively they approximate a random sampling of people residing in a particular study area (2009 REA, section 8.2).

Each simulated individual is assigned a sequence of activity events[16] consistent with the individual's demographic characteristics and accounting for effects of day types (e.g., weekend, weekday) and outdoor temperature on daily activities. APEX calculates the concentration in the microenvironment associated with each event in an individual's activity pattern and aggregates the event-specific exposures within each hour to obtain a continuous time series of hourly exposures spanning the time period of interest. Each activity is associated with an energy expenditure rate, and commonly quantified as a multiple of the resting metabolic rate using metabolic equivalents (METs).[17] The MET is then used with individual-specific information (e.g., age, body mass and surface area) to characterize the ventilation rate and exertion level for the individual during each activity and associated exposure event.[18] Based on this tracking of activity level, APEX provided estimates of individuals' 5-minute maximum SO_2 exposure concentrations during particular exertion levels[19] of interest for the assessment, e.g., moderate or greater exertion (2009 REA, section 8.9).

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[16] Daily activity patterns for individuals in a study area, an input to APEX, are obtained from detailed diaries that are compiled in the Consolidated Human Activity Database (CHAD) (McCurdy et al. 2000; U.S. EPA, 2002; 2009 REA, section 8.5).

[17] The term MET comes from the phrase "metabolic equivalents of task" (2009 REA, Appendix B).

[18] In the 2009 REA, an equivalent ventilation rate (EVR) was calculated to identify a level at which any individual (child or adult) could be considered at or above exertion levels of interest. This was needed because lung volumes (and hence relative ventilation rates) vary with factors such as body size and the controlled human exposure studies only used adult subjects. An EVR at or above 22 L/min-m^2 (children or adults) was identified as a moderate or greater exertion rate corresponding to the adult ventilation rate of approximately 40-50 L/min at which effects were observed in the controlled human exposures studies (as summarized in section 2.2.3 above). The EVR is derived by normalizing the simulated individuals' activity-specific ventilation rate ($\dot{V}_E$) to their body surface area (2009 REA, sections 8.5.5 and 8.8.2).

[19] As summarized in section 2.1.3 above, the exertion levels at which effects have been observed in controlled human exposure studies are generally characterized as moderate or heavy.

Key aspects of the APEX modeling as applied in the 2009 REA are described in the sections below.

2.3.2.1 Air Concentrations

The SO_2 concentrations in ambient air on which the APEX exposure estimates are based have several components: (1) use of AERMOD, a steady-state Gaussian plume model, to provide the spatial and temporal characterization of 1-hour SO_2 concentrations for the two modeling domains; (2) estimation of twelve 5-minute concentrations for each hour; and (3) representation of the eight air quality scenarios (described in section 2.2.2 above).

AERMOD was used to estimate 1-hour SO_2 concentrations in ambient air using emission estimates from stationary, non-point, and port sources (additional detail on aspects of the air quality modeling is available in section 8.4 of the 2009 REA). Meteorological data, processing methodologies used to derive input meteorological fields (e.g., temperature, wind speed, precipitation), and information on land use and surface characteristics were used to determine pollutant dispersion characteristics, atmospheric stability, and mixing heights. The emission sources modeled included: major stationary emissions sources within the domain; major stationary sources outside the domain having the potential to affect air quality (cross-border stacks); non-point source area emissions; emissions from ports; and background sources not otherwise captured.[20] One-hour average concentrations of SO_2 were estimated at ambient air monitoring locations (where available) and census block centroids in each study area. The full annual time series of hourly concentrations were estimated for 2002 by summing concentration contributions from each of the emission sources at each of the defined air quality receptors.

Five-minute maximum SO_2 concentrations were estimated for each AERMOD-predicted 1-hour concentration using the empirically-derived PMRs (developed from recent 5-minute SO_2 ambient air monitoring data, as described above in section 2.1.4). These 5-minute maximum SO_2 concentration estimates were then used to estimate the 11 other 5-minute SO_2 concentrations that occurred within every hour. To simplify the approach, the 11 other 5-minute SO_2 concentrations in each hour were set equal to each other, at a level corresponding to the 1-hour mean when considering the estimated 5-minute maximum concentration. While the occurrence of multiple peak concentrations above benchmark levels within an hour is possible, it was assumed that use of the twenty-four 5-minute maximum SO_2 concentrations generated each day would provide an accurate estimate of the maximum exposure that an individual might experience in a day. The additional eleven 5-minute concentrations within an hour at each receptor were approximated using an algorithm in APEX that considered the 1-hour SO_2 concentration, the appropriate PMR,

[20] Not all emission source categories were present in both modeling domains.

and the estimated 5-minute maximum SO_2 concentration at the receptor (2009 REA, section 8.7.1). This spatially complete (at the block level) and consecutive time-series of 5-minute SO_2 concentrations served as the ambient air concentrations input to algorithms within APEX that estimate the microenvironmental concentrations.

To reduce processing time and for other computational reasons, the approach used in the exposure-based assessment to reflect the various air quality scenarios was different than that used in the air quality-based assessment (section 2.2.1). Instead of proportionally adjusting the 1-hour ambient air concentrations using a multiplicative factor as was done for the air quality-based assessment, the exposure-based assessment adjusted the breakpoints for the exposure model output bins (see section 2.3.2.5 below) by that same adjustment factor. This provided the counts of individuals for all exposures of interest (for purposes of both the benchmark comparison and lung function risk calculation) considering each of the different air quality scenarios (described in Table 2-1). The result of this approach is mathematically equivalent to the more computationally extensive alternative of running APEX repeatedly with datasets of adjusted air quality for each of the air quality scenarios (2009 REA, section 8.8.3 and Figure 8-14).

2.3.2.2 Simulated Populations

Exposures were estimated for individuals of all ages with asthma, and for a subset of that population group, children with asthma. Representative profiles of hypothetical individuals were developed for the exposure modeling simulation by taking into account age- and sex-specific population counts and employment probability estimates, asthma prevalence rates, and home-to-work commuting locations and probabilities. Characteristics of the simulated individuals (e.g., body surface area, BSA) and the activities in which they engage were used in APEX to generate activity-specific ventilation rates and to characterize when simulated individuals were at moderate or greater activity levels. The information on which such characteristics of the simulated population were based are described briefly below and in more detail in section 8.5 of the 2009 REA.

- *Population Counts and Employment Probabilities:* Block-level population counts were obtained from the 2000 Census of Population and Housing Summary File. Employment estimates were developed from census information (U.S. Census Bureau, 2007) and were separated into age and sex groups.[21] The total population simulated within the Greene County and St. Louis modeling domains was approximately 1.4 million persons, with over 360,000 children.

[21] Children under the age of 16 were assumed not to be employed. Additionally, it was assumed that employment probabilities for a census tract applied uniformly to the constituent census blocks. More detail is provided in Appendix B.2.2.2 of the 2009 REA.

- *Asthma Prevalence:* The proportion of the population of children characterized as having asthma was estimated by statistics on asthma prevalence rates that had been recently used in the 2008 review of the O_3 NAAQS (U.S. EPA, 2007). Age and sex specific asthma prevalence rates for children were generated from an analysis of data in the 2003 National Health Interview Survey (CDC, 2007). Adult (i.e., >18 years old) asthma prevalence rates were stratified by sex and based on Missouri regional data (MO DOH, 2002). The asthma prevalence rates by age and gender used in Greene County and St. Louis exposure modeling are summarized in Table 8-7 in the 2009 REA.
- *Commuting Database:* Commuting data were derived from the 2000 Census, collected as a part of the Census Transportation Planning Package (U.S. DOT, 2007). The data on counts of individuals commuting from home-to-work locations at a number of geographic scales were used with finely resolved land use data to derive estimates of the frequency of commuting to workplace outside the census block of residence (2009 REA, section 8.5.3).[22]
- *Body Weight and Surface Area:* Each simulated individual's body mass was assigned based on random sampling of age- and gender-specific body mass distributions from the 1994-2004 National Health and Nutrition Examination Survey (NHANES). Age- and sex-specific BSA was then estimated for each simulated individual based on previously developed logarithmic relationships using body mass as an independent variable (2009 REA, section 8.5.4).
- *Activity-Specific Ventilation Rates:* The ventilation rate for a given activity in which a simulated individual engaged is derived from the energy expenditure rate of the activity and an algorithm for estimating the volume of air expired per minute based on the rate of oxygen consumption as well as the age and sex of the individual (Graham and McCurdy, 2005; 2009 REA, section 8.5.5).

2.3.2.3 Human Activity Patterns

To estimate individuals' exposure to pollutants, APEX relied on detailed information on the patterns of time spent in different microenvironments drawn from several large-scale databases of human time-activity-location patterns, the most comprehensive of which is the Consolidated Human Activity Database (CHAD).[23] Time-activity pattern data from studies included in this database, typically consists of a sequence of location/activity combinations spanning 24-hours, with 1 to 3 diary-days of data for any single study individual. In order to simulate individuals' activities over a full year, long-term multi-day activity patterns were estimated from single days by combining daily records from the same or similar person using important person-level (age, sex) and other (day of week) attributes that influence activity

[22] Travel on roads (e.g., via car, bus, rail) was also simulated for other individuals (e.g., unemployed, children, persons working at home), but with the vehicle travel simulated to occur within the block where the individual resides (2009 REA, section 8.5.3).

[23] The current CHAD is available and described at: https://www.epa.gov/healthresearch/consolidated-human-activity-database-chad-use-human-exposure-and-health-studies-and

patterns and an algorithm designed to account for intra- (day to day) and inter- (across simulated population) personal variability. The algorithm first used a cluster analysis to group similar daily activity patterns records (generally about 2-3 cluster groups), each stratified by day-types and person-level attributes of interest. Then, transition probabilities (i.e., frequencies of having one cluster group follow another) for each stratification are calculated and used to construct a long-term sequence for each simulated individual (2009 REA, Appendix B).

2.3.2.4 Microenvironmental Concentrations

Concentrations of SO_2 from ambient air occurring in the microenvironment associated with each activity contribute to the individual exposure events that together make up a simulated individual's exposure. Concentrations were estimated for 12 different microenvironments based on ambient air pollutant concentration and factors such as penetration, air exchange rate, and pollutant decay or decomposition rate. A mass balance approach was generally used for estimating concentrations for indoor environments and a factor-based approach was used for outdoor and in-vehicle microenvironments (2009 REA, section 8.7 and Appendix B).

2.3.2.5 Exposure Estimates

The APEX model calculates exposure as the time-series of microenvironmental concentrations that a simulated individual experiences as determined by the combination of the individuals' activity patterns, the ambient air concentrations, and microenvironmental factors. In the 2009 REA, with the focus on 5-minute maximum concentrations, exposure was derived as a time-series of 5-minute exposure concentrations.[24] Other APEX outputs were also used to characterize the exposure circumstances contributing to 5-minute exposures of interest. For example, tabulation of the 5-minute microenvironment concentrations in the *as is* (unadjusted) scenario provided information on the type of microenvironments contributing to the highest exposures (e.g., indoors, outdoors, vehicles). The 5-minute exposure estimates for the *as is* air quality scenario indicate that maximum 5-minute exposures occurred much more frequently outdoors (versus indoors), at all exposure levels (2009 REA, Figure 8-21).

The time series exposure data for all modeled individuals considering each air quality scenario were statistically summarized and tabulated to calculate two general types of exposure estimates: (1) counts of the estimated number of people whose exposure exceeded a specified SO_2 concentration level one or more times in a year and the number of times per year that they

[24] Consistent with the magnitude of adjustment for each air quality scenario, the exposure estimates for *as is* (unadjusted) air quality in the two study areas were similar to the results for air quality adjusted to just meet potential alternative standards of 50 and 100 ppb, in terms of the 99th percentile 1-hour daily maximum, averaged over three years (2009 REA, Figures 8-16 and 8-19).

are so exposed; and (2) the number of times per year a person is so exposed in terms of person-occurrences or person-days.[25,26] The former highlights the number of individuals with the various levels of exposures; APEX can also report counts of individuals with multiple such exposures. The person-occurrences metric estimates the number of times per simulation period that various levels of exposure are experienced and then accumulates these estimates for each simulated population in the modeling area.

2.3.3 Health Risk Characterization

The APEX outputs described in section 2.3.2.5 above were used to develop two different types of risk metrics for each of the air quality scenarios, one involving comparison of exposures to benchmark levels and the second using exposures to estimate risk of lung function decrements (2009 REA, chapters 8 and 9). The exposure-to-benchmark comparison characterizes the extent to which individuals in at-risk populations could experience exposures of potential concern (i.e., concentrations above specific benchmarks while at moderate or greater exertion levels). The lung function risk analysis provides estimates of the extent to which at-risk populations could experience decrements in lung function. As the two types of metrics differ in their strengths and limitations, use of both metrics allowed for a more robust risk characterization.

The results for the comparison to benchmark metrics were characterized in the following ways:

- number and percent of individuals in the simulated at-risk population exposed at or above the benchmark levels of 100, 200, 300, and 400 ppb, while at moderate or greater exertion, at least once per year; and
- total number of days in a year that any individual in the simulated at-risk population was exposed while at moderate or greater exertion, at or above selected benchmark levels.

These results are described in detail in the 2009 REA (section 8.9 and Appendix B.4).

Lung function risk was estimating by applying the E-R functions to the binned exposure estimates (i.e., numbers of simulated individuals with daily maximum 5-minute exposures in the

[25] For the purpose of evaluating risk using benchmark levels and decrements in lung function, the estimated 5-minute exposure concentrations were first tabulated into bins considering 50 ppb increments ranging from 0 to 800 ppb by 50 ppb increments. Then, based on the individual's breathing rate associated with each concentration, the risk characterization then focused on exposures experienced while at or above moderate ventilation rates. The results for exposures associated with moderate or higher ventilation rate were used in developing the two types of risk metrics described in section 2.3.3.

[26] An individual with an equivalent ventilation rate (EVR) at or above 22 L/min-m^2 (children or adults) for a 5-minute exposure event was characterized as performing activities at or above a moderate ventilation rate (as summarized in section 2.4.2). Since there were limited controlled human exposure study data available for children with asthma, this ventilation target is based on normalizing (by body surface area) the ventilation rate for adults observed to experience effects from 5-10 minute SO_2 exposures in many of the controlled human exposure studies (which was approximately 40-50 L/min) (2009 REA, section 8.8.2).

binned range). As the E-R functions are in terms of percent of exposed individuals exhibiting a particular magnitude of response (e.g., ≥ 100% and ≥ 200% increase in sRaw), the results for the lung function risk metric were characterized in the following ways:

- number and percent of individuals in the simulated at-risk population expected to experience one or more of two defined levels of lung function response in a year (i.e., ≥ 100% and ≥ 200% increase in sRaw, ≥ 15% and ≥ 20% decrease in FEV_1); and
- estimated total number of expected occurrences of the two defined levels of lung function response in individuals in the simulated at-risk population.

These results are described in detail in the 2009 REA (section 9.3 and Appendix B.4).

Similar differences were observed between the two study in the various results and were concluded to be likely indicative of the different types of study area locations they represented. Greene County is a rural county with much lower population and emission densities, compared to the St. Louis study area which has population and emissions density similar to other urban areas in the U.S. (2009 REA, section 8.9.2) Therefore, there would likely be more exposures in St. Louis, and greater numbers and percentages of people with asthma at elevated ventilation rates experiencing moderate or greater lung function responses compared to the Greene County study area (which is what the results indicated). Thus, the 2009 REA concluded that the St. Louis results were concluded to be more informative than the Greene County results for the purpose of assessing the adequacy of the then-existing standards and in considering potential alternative standards with regard to the protection provided against effects linked to 5-minute exposures. Further, the EPA staff judged that that the exposure and risk estimates for the St. Louis study area provided useful insights into exposures for other urban areas in the U.S. with similar population and SO_2 emission densities (74 FR 64827, December 8, 2009).

2.3.4 Key Uncertainties and Limitations

The aspects of the exposure-based assessments contributing uncertainty to the results are summarized here. These uncertainties are also discussed in Chapter 3, in the context of considering information newly available in this review and the potential impact of its use on the results of a new assessment. Areas of uncertainty below are grouped with regard to the different modeling elements (more detail is available in sections 8.11.2, 9.3 and 9.4 in the 2009 REA).

Air Quality Modeling and Ambient Air Concentration Estimates

- *Emissions profiles:* Point source emissions, including temporal and spatial profiles, were concluded to contribute a low level of uncertainty to air quality estimates. With regard to area source emissions, there was a lack of detailed information regarding spatial, temporal aspects and height of releases. Use of a derived area source emissions profile (in place of the default profile) improved model performance, reducing uncertainty in the 1-hour SO_2 concentration predictions. In the absence of actual local source emission profiles, however, this modeling step remained an important uncertainty.

- *AERMOD 1-hour concentrations:* Model-to-monitor comparisons indicated reasonable agreement. Most of the overestimations in 1-hour concentration occurred at the lowest concentrations, which would be expected to limit the magnitude of influence this uncertainty would have on estimated peak 5-minute concentrations. The spatial representation of 1-hour ambient air concentrations using AERMOD was considered a better representation than could have been developed from the limited number of ambient air monitors.
- *Air quality adjustment procedure:* To derive the air quality conditions for each air quality scenario, the proportional adjustment factors derived from a study area's design value were applied to adjust all ambient air monitors in the study area. Deviation from the proportionality within the study area could result in over- or under-estimation of SO_2 concentrations. The decision to use the proportional approach was based on analyses which indicated it to be a reasonable approach for simulating higher concentrations at most monitoring sites since, historically, concentrations have decreased linearly across the entire concentration distribution. However, the uncertainty about future source emissions control scenarios is unknown (2009 REA, section 7.4.2.5).
- *Selection of 5-minute averaging time for concentrations to compare to benchmark levels:* The SO_2 exposure durations in the controlled human exposure studies were generally between 5 and 10 minutes. The evidence indicates that onset of symptoms occurs within minutes in response to the study exposure concentrations, indicating responsiveness to the "peak" concentration encountered (2008 ISA, section 3.1; U.S. EPA, 1994, section 4.1). Further, there was general consistency in the observed responses for 5-minute and 10-minute exposures to the same concentration.
- *Statistical model used for estimating 5-minute SO_2 concentrations:* A number of uncertainties were identified regarding the statistical model developed and used to estimate 5-minute concentrations and its impact on the assessment results. These uncertainties included the impact from how the PMR data were screened; the temporal representation of data used in the statistical model development; the form of the distribution used to represent the PMRs; the accuracy of the model in predicting daily 5-minute maximum concentrations; and the reproducibility of the model predictions (2009 REA, section 7.4.2.6).

Exposure Modeling and Exposure Concentration Estimates for At-Risk Populations

- *Microenvironmental concentrations:* Concentrations of SO_2 were estimated in 12 microenvironments based on data regarding air exchange rates, air conditioning prevalence, and indoor removal rates. The air exchange rates used were not specific to the study areas, although the air conditioning prevalence data were specific to St. Louis. The data for indoor removal rate of SO_2 were from a review of SO_2 removal rates in the extant literature but many assumptions were required to develop the removal rate distributions that were used. Most peak exposures occurred outdoors, although it was recognized that maximum 5-minute indoor exposures could be underestimated when not using the full set of varying 5-minute concentrations within each hour.
- *Simulated at-risk populations:* Population demographic data for each study area were taken into account in APEX to develop study area population profiles. These profiles were developed using data on population counts and employment probabilities, asthma

prevalence, commuting patterns, body surface area, and activity-specific ventilation rates. These data were from reliable, quality assured sources, and the uncertainty associated with these data was judged to be low.

- *Human activity patterns:* Typical time-activity patterns data were available from a reliable, quality assured source and were available in the published literature. While most data in the database were expected to have a low magnitude of influence on the uncertainty, having a limited number of diaries could limit our ability to represent variability time expenditure for population groups of interest, potentially leading to instances of under- or over-estimating health risks.

- *Estimation of 5-minute exposure concentrations:* The statistical model used in calculating 5-minute SO_2 ambient air concentrations – and microenvironment concentration estimation (see above) – was associated with some uncertainty, of unknown magnitude, given the relatively few monitors having such data and their limited geographic range. This uncertainty contributes uncertainty to the 5-minute exposure estimates. The lack of empirical 5-minute SO_2 personal exposure data precluded a model-to-monitor evaluation for the 5-minute SO_2 exposures estimated by APEX.

Comparison to Benchmarks

- *Benchmark Concentrations:* For the benchmark levels at or above 200 ppb, there is generally lower uncertainty (than for lower levels) with regard to what is quantified (e.g., exposure concentrations at which effects to people with asthma can occur), although the lung function response can vary considerably among individuals (74 FR 64823, December 8, 2009). The health effects information is limited with regard to identification of exposures that elicit the selected lung function responses in individuals having severe asthma. The recognition of a potential for moderate or greater decrements in lung function at levels below 200 ppb (given that approximately 5-30% of exercising subjects with asthma experienced moderate or greater decrements in lung function following exposure to 200-300 ppb SO_2, the lowest levels tested in free-breathing chamber studies), was addressed through the inclusion of a 100 ppb benchmark level. The lack of free-breathing chamber studies below 200 ppb, however, contribute uncertainty to interpretation of results related to the 100 ppb level.

Lung Function Risk Model and Response Estimates

- *Estimating lung function response for exposures lower than studied:* While there is strong controlled human exposure study evidence for SO_2 eliciting lung function responses within the range of tested 5-10 minute exposures (i.e., $\geq$ 200 ppb) and as low as 100 ppb (where SO_2 was administered via mouthpiece), there is uncertainty about whether SO_2 is causally related to lung function effects at exposure levels below 100 ppb. Because this risk assessment approach assumes no threshold, there is uncertainty associated with health risk estimated using exposures below 100 ppb. As a means of informing uncertainty in estimates at lower exposures, the 2009 REA reported risk estimates for two E-R functions based on two different statistical models (2-parameter logistic and probit). An analysis of the contribution to the estimated risk using both of these functions indicated that 5-minute maximum exposures at or below 100 ppb contributed substantially to the risk estimates for the lowest alternative standard air quality scenarios (more so for the logistic function), such as those for daily maximum 1-hour standard

levels of 50 and 100 ppb (2009 REA, Figures 9-7 and 9-8), levels which are just below and above the current standard.

- *Limitations of the available exposure-response data:* As described in section 2.2.4, the subjects in the controlled human exposure studies were people with mild and/or moderate asthma, contributing uncertainty with regard to the extent to which responses of more severely asthmatic individuals are represented, which may lead to some risk underestimation. Additionally, use of E-R relationships from studies involving adult subjects with asthma to estimate risk for all people with asthma, including children, contributes somewhat greater uncertainty to the child risk estimates. Few data have been collected for children with asthma, although limited evidence for adolescents (from studies that administered SO_2 via mouthpiece) indicate similar respiratory effects as adults at similar SO_2 exposures (2008 ISA, section 3.1.3.5).
- *Exposure history:* While data are lacking for SO_2, data for other pollutants (e.g., ozone) indicate that prior exposures to the pollutant may lead to either enhanced or diminished lung function responses depending on the exposure pattern. The 2009 REA assumed that each SO_2-induced response was unaffected by any prior SO_2 exposures. Uncertainty associated with this approach was concluded to be low.
- *Effect of co-exposure to other pollutants on SO_2-related lung function response:* There is some evidence (e.g., experimental animal studies) of increased response to SO_2 exposures occurring in the presence of other common pollutants (e.g., PM), although controlled human exposure studies of using simultaneous exposures to multiple pollutants are lacking. The 2009 REA did not address a potential effect of co-exposures to other pollutants.

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3 CONSIDERATION OF THE NEWLY AVAILABLE INFORMATION

In this chapter, we consider the extent to which our characterization of exposure and risk in the last review of the primary SO_2 standard may remain appropriately informative to the key questions in the current review, as summarized in the IRP. As noted in that document, the ISA, REA (if warranted) and PA developed in this 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 existing primary SO_2 standard (IRP, section 3.2). Accordingly, this chapter considers the extent to which a new assessment of exposure and risk is warranted to provide an adequate characterization of human exposure and risk, particularly with regard to the existing standard, based on the currently available information in this review.

The first section below (section 3.1) provides an overview of key considerations. The subsequent sections are organized around key components of the exposure and risk assessments from the last review with particular attention given to limitations and sources of uncertainty, as described in sections 2.2.4 and 2.3.5 above, and the extent to which they may be addressed by the information newly available in this review (e.g., data, new technical insights, modeling approaches). Section 3.2 focuses on key aspects of the currently available health effects evidence and section 3.3 focuses on information pertaining to our characterization of the pertinent ambient air concentrations. Section 3.4 addresses estimation of population exposure and risk. Discussion of this information and preliminary conclusions regarding the extent to which a new exposure and risk assessment is warranted in the current review are presented below in section 3.5.

3.1 KEY CONSIDERATIONS

In any NAAQS review, the considerations contributing to a decision to conduct a new exposure and risk assessment will necessarily be particular to the circumstances pertaining to the subject pollutant, including the role played by the exposure and risk information in the EPA's previous decisions on the existing standard and the role of exposure and risk information expected in the current review. Another important consideration is the robustness of the exposure and risk estimates for the existing standard that are available from the last review. In reaching a decision on conducting a new REA, in addition to such policy-relevant considerations, we also consider the extent to which results of a new quantitative exposure and risk assessment are expected to appreciably change our understanding of exposures and risk beyond the insights gained from the assessments from the last review. More specifically, we consider questions such as the following:

- Does the information newly available in this review appreciably change key aspects of our conceptual model for exposure and risk assessment that was developed for the last review?
- Would the newly available information contribute to appreciably changed inputs for that model?
- Would such changes be expected to appreciably improve our characterization of exposure and risk associated with the existing standard?

With regard to the first question, section 3.2 below considers the health effects information in the second draft ISA and whether it continues to support the conceptual model developed in the last review (summarized in section 1.2). Based on the conclusion in section 3.2 that these aspects of the conceptual model from the last review remains appropriate, the subsequent sections focus on key areas in the conceptual model and aspects of them that play critical roles in our characterization of exposure and risk. Particular attention is given to consideration of the availability of new information pertaining to those aspects, and the extent to which it might be expected to substantially address key areas of uncertainty in the last review.

Additionally, with regard to our understanding of exposure and risk associated with air quality conditions under the existing standard, we note that the 2009 REA did not include an air quality scenario for conditions associated with the existing standard of 75 ppb, as a 99th percentile daily maximum 1-hour average (see Table 2-1). In considering the REA estimates in the 2010 decision, the Administrator recognized that risks for the new standard would be expected to fall somewhere between the estimates developed for the potential alternative standards of 50 and 100 ppb, as a 99th percentile daily maximum 1-hour average, averaged over three years (75 FR 35520). Thus, we recognize that a decision to develop a new REA in the current review would, at a minimum, provide an estimate specific to the conditions associated with the existing standard as an alternative to relying on the range of estimates for the 50 ppb and 100 ppb potential standard levels from the last review, or considering development of estimates using an interpolation method.

3.2 HEALTH EFFECTS INFORMATION

The primary conclusions based on the assessment of the currently available health effects evidence in the second draft ISA, including that newly available in this review, are largely consistent with the conclusions reached in the 2008 ISA. More specifically, the second draft ISA for this review continues to conclude that respiratory effects in individuals with asthma are causally related to short-term SO_2 exposures, finding the evidence for relationships with other health effects and exposure durations to be suggestive or inadequate (second draft ISA, pp. l-lii). While the evidence base in this review includes some newly available studies, the primary

conclusions on respiratory effects in individuals with asthma continue to be based largely on the collection of controlled studies of peak (5-10 minute) exposures of persons with asthma that were included in the 2008 ISA (second draft ISA, pp. l-lii). These studies provided the primary basis for the 2009 REA.

The sections below focus on several key aspects of the conceptual model developed for the 2009 REA: (1) at-risk populations, (2) exposures of concern and characterization of E-R relationships for lung function decrements, and (3) other health endpoints and associated risk metrics. In the sections below, we assess the extent to which the currently available health effects information supports or indicates the need for adjustment to how these aspects of the conceptual model were addressed in the 2009 REA. In so doing, we also consider the extent to which the information now available might address limitations or areas of uncertainty related to these aspects, and contribute to an appreciably improved and different quantitative characterization of exposure and risk.

3.2.1 At-Risk Populations

In the second draft ISA for this review, the population concluded to be at increased risk of effects from SO_2 exposure continue to be people with asthma, including particularly children with asthma (second draft ISA, section 6.3.1). The second draft ISA concludes that the evidence is more limited for other populations potentially at risk (second draft ISA, section 6.6). Thus, the currently available health effects evidence, including that newly available in this review, does not suggest the need for changes to the populations included in the conceptual model for SO_2 exposure and risk assessment.

3.2.2 Lung Function Decrements

In the last review, within the evidence for respiratory effects, the category of effects concluded by the ISA to be causally related to short-term SO_2 exposure, the body of controlled human exposure studies provided a strong foundation for quantitatively assessing lung function decrements using benchmark exposure levels and quantitative exposure-response information, as summarized in section 2.1.3 above (2009 SO_2 REA sections 6.2 and 9.2). The information available in the current review, including that newly available, continues to provide strong support for these components of the REA conceptual model, including their emphasis on peak exposures, e.g., 5-minute duration (second draft ISA, section 5.2.1.2). Additionally, the information available in the current review, as presented in the second draft ISA, does not include new information for the sources of uncertainty identified for these approaches in the 2009 REA (summarized in section 2.2.4 and 2.3.5 above).

Although no new studies are now available to address the key uncertainties, we have additionally considered the potential use of additional, previously available data, as well as

additional methods, primarily related to derivation and application of the functions for lung function decrement. Specifically, data are available from controlled human exposure studies that were not used in the development of the E-R functions for the 2009 REA (Linn et al., 1983; Horstman et al., 1986; see section 4.2.4). While the addition of these data to the dataset from which the E-R functions are derived would not be expected to substantially change the shapes of the functions used in the last review, it could reduce uncertainty and increase our confidence, particularly in estimates based on application of the functions within the range of the controlled human exposure study data. With regard to additional methods or analyses, new sensitivity analyses could be performed in consideration of the application of the E-R function to exposures below those for which study data are available (e.g., below 100-200 ppb). Such analyses could explore alternative functions, informing our understanding of the impact of this source of uncertainty on the risk estimates (see section 4.2.4).

3.2.3 Other Endpoints

In developing the conceptual model for the 2009 REA, we considered the strength of the health effects evidence for an array of respiratory effects, the category of effects that the ISA concluded were causally linked to short-term SO_2 exposure. In addition to the strong foundation for quantitatively assessing lung function decrements (as discussed in section 3.2.2 above), there was some information from epidemiological studies for a number of other related health outcomes (e.g., emergency room visits and hospital visits for asthma episodes). However, the number of studies in U.S. cities was limited and, where co-pollutant models were analyzed, the inclusion of other pollutants (e.g., PM_{10}) often resulted in a loss of statistical significance for SO_2. Thus, the information was concluded to be inadequate for developing quantitative risk estimates (2009 REA, section 6.3).

Within the information newly available in this review, only a limited number of new studies focused on such asthma exacerbation-related effects have been identified that might provide information on concentration-response relationships potentially useful in a quantitative risk assessment. These studies are within the epidemiological evidence, with the most cohesive evidence coming from studies on asthma-related emergency department visits (e.g., Strickland et al. 2010; Byers et al. 2015; Alhanti et al. 2015; Li et al. 2011; second draft ISA, section 5.2.1). None of these new studies, however, would address the limitations and uncertainties identified in the last review with regard to their use in a quantitative risk assessment (e.g., potential co-pollutant confounding) (Appendix A). Therefore, as was the case in the last review, the currently available evidence does not support conducting a quantitative risk assessment for these other health endpoints because of the limited utility of associated estimates in the decision-making process given the nature of the uncertainties associated with these studies.

3.3 AMBIENT AIR CONCENTRATIONS

The characterization of ambient air concentrations is an essential component in the characterization of exposure and risk associated with SO_2 in ambient air. In the 2009 REA, this characterization involved reliance on a combination of air quality modeling and ambient air monitoring data. In the exposure assessment, air quality modeling was used to characterize the spatial and temporal distribution of 1-hour concentrations while 5-minute concentrations, a critical influence on the 5-minute exposure estimates, were estimated through application of a statistical model based on the limited number of monitors at which both hourly and associated maximum 5-minute concentrations were available, as summarized in section 2.1.4 above. The sections below consider the information newly available in this review with the potential to appreciably improve these estimates.

3.3.1 Estimation of 5-Minute Concentrations

In the last review, a key uncertainty with respect to the air quality characterization was the limited availability of 5-minute SO_2 monitoring data (as summarized in section 2.1 above and described in more detail in the 2009 REA). More specifically, 5-minute SO_2 concentrations were available through 2006 (the most recent year for which complete monitoring data were available) from a relatively small number of monitors (Figure 3-1). Since that time, more 5-minute data are available as a result of the regulatory requirements promulgated in 2010 as part of the last SO_2 NAAQS review (Figure 3-1).[27] Although 5-minute data were available for fewer than 10% of monitoring sites at the time of the last review, such data (either all 12 values in each hour or just the maximum 5-minute concentrations) are currently available for nearly 90% of the approximately 400 sites nationwide, providing a more robust foundation for characterization of 5-minute ambient air concentrations in this review.

Further, the newly available monitoring data also include an even greater improvement in the number of monitors reporting the 12 consecutive 5-minute concentrations for each hour (Figure 3-1). In the recent period, such data are available for approximately 40% of all monitors. The lack of this information for the 2009 REA, which precluded the representation of the full variation in 5-minute concentrations within an hour, was an area contributing uncertainty to the 2009 REA exposure estimates (section 2.3.5). Thus, incorporation of each hour's full series of 5-minute concentrations into the overall modeling approach supporting the 5-minute exposure estimates (in addition to the reliance on a more robust 5-minute concentration dataset overall)

[27] At SO_2 NAAQS compliance sites, air monitoring agencies are now required to report, for every hour of the day, 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 (75 FR 35554, June 22, 2010).

would be expected to reduce two areas of uncertainty associated with the 5-minute ambient air concentration estimates.

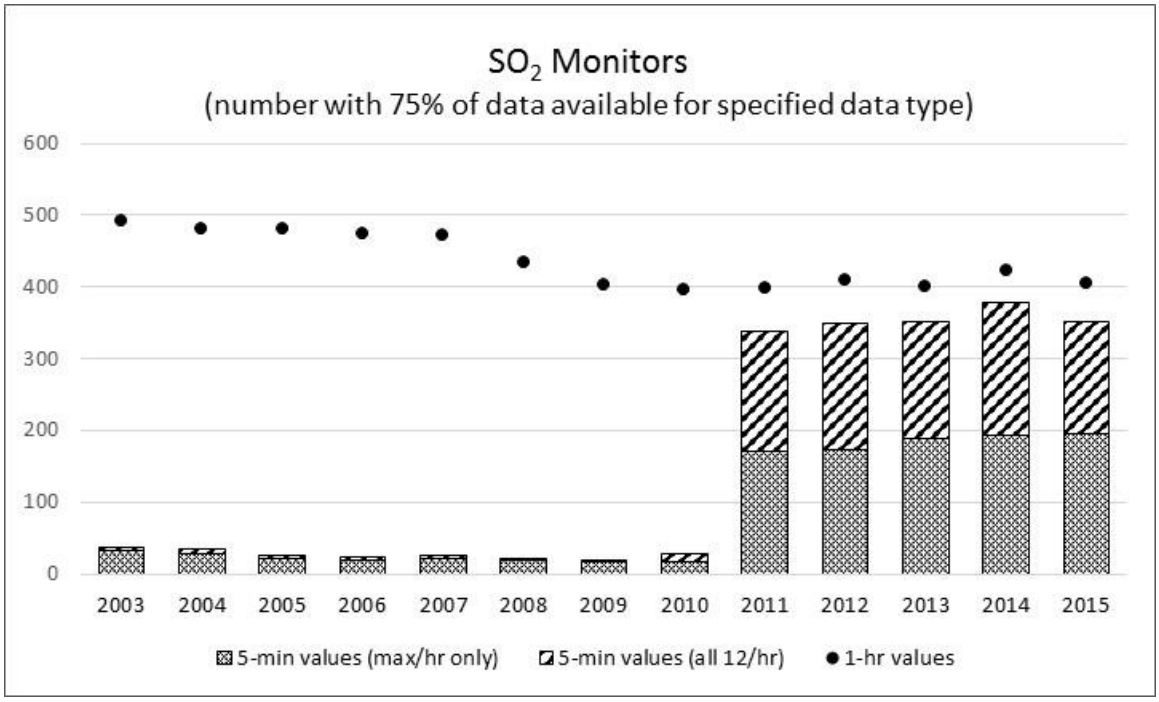

Figure 3-1. Trend in number of monitors with 5-minute data.

Preliminary analyses of the now-expanded monitoring dataset better define the relationship between 1-hour concentrations of SO_2 in ambient air (and monitor design values based on the current 1-hour standard) and the occurrence of maximum of 5-minute concentrations of interest. For example, analysis of these data for the years[28] 2013 to 2015 indicates that among monitors with design values at or below 75 ppb, the number of days with maximum 5-minute concentrations above 200 ppb ranged from zero to 22 (Appendix B). We note that interpretation of these results with regard to potential exposure and risk is limited, however, without consideration of factors influencing exposure (e.g., spatial variability in ambient air concentrations which might not be captured by the monitoring network, spatial/temporal variability in human activity patterns and breathing rates of potentially exposed individuals), as can be done in the context of an exposure-based assessment.

[28] We note that the 1-hour SO_2 dataset analyzed was limited to monitors and years for which the 1-hour data met 75% completeness criteria. The completeness of the maximum 5-minute concentrations varied in the number of monitors and years for which data were available. However, given the limited amount of 5-minute data available, completeness criteria were not applied to the maximum 5-minute SO_2 concentrations in the interest of maximizing sample size for the analysis. Consequently, at monitors with incomplete datasets, the number of days with peak concentrations of interest may also have been incomplete.

3.3.2 Characterizing the Spatial and Temporal Distribution of 1-hour SO_2 Concentrations

The exposure-based assessment in the 2009 SO_2 REA relied on air quality modeling using the air dispersion model, AERMOD, to estimate 1-hour concentrations across each study area over the years assessed for each air quality scenario. The current information continues to support the use of an air dispersion model such as AERMOD over the use of other models, such as photochemical models, for modeling of directly emitted SO_2 concentrations for use in assessing risk and exposure for this pollutant. Unlike dispersion models, photochemical models cannot capture the sharp concentration gradients that can occur near SO_2 sources. Also, SO_2 emissions to ambient air are dominated by point sources, such as large coal-fired utilities, and AERMOD is the EPA's preferred air quality model for SO_2 for State Implementation Plans (SIPs)[29] and new source permitting purposes. For all of these reasons, AERMOD remains the most appropriate model for predicting SO_2 concentrations in ambient air.

Since the last review, there have been a number of changes to the AERMOD modeling system which includes the AERMOD dispersion model itself, and associated data processors, including the AERMET meteorological preprocessor, and the AERMAP terrain processor. Specifically, there have been ten updates to the AERMOD model, six updates to AERMET, and one update to AERMAP (U.S. EPA, 2016). There has also been the development of AERMINUTE, a preprocessor to AERMET that calculates hourly average winds from 1-minute ASOS winds at NWS stations (U.S. EPA, 2015). Some of these model changes are considered major improvements and, in some instances, could significantly affect results (e.g., use of hourly averaged winds from AERMINUTE, options for treatment of low wind situations, and treatment of building downwash for stacks exceeding Good Engineering Practice (GEP) stack heights, among others). How they might affect the results will vary depending on the particular feature. For example, model changes could lead to increased concentrations at the upper percentiles of the concentration distribution (such as use of AERMINUTE or treatment of building downwash for stacks exceeding GEP). In other instances, the model changes, such as options for treatment of low wind speeds (adjusted surface friction velocity) could lead to a decrease in concentrations at the higher end of the concentration distribution.

3.4 EXPOSURE ESTIMATES

Exposure considerations are another essential component in the characterization of exposure and risk associated with SO_2 in ambient air. Such considerations include the factors that affect exposures that are not addressed by consideration of ambient air concentrations as a

[29] With regard to such plans, the Clean Air Act requires states to develop a general infrastructure plan to provide for attainment and maintenance the NAAQS in all areas of the country, and a specific plan to provide for attainment of the NAAQS for any area that has been designated as nonattainment for a NAAQS.

surrogate for exposure to SO_2 from ambient air. In addition to the attenuation in SO_2 concentrations expected to occur in microenvironments and the influence of human activity patterns on exposure concentration, accounting for human physiology and the occurrence of elevated ventilation rates concurrent with SO_2 exposures is key to characterizing health risk for SO_2. This section focuses on areas of key uncertainty and limitations in the exposure assessment for the 2009 REA for which there is newly available information, tools or approaches, and considers the extent to which there is new information that might be expected to improve our estimation of SO_2 population exposure.

3.4.1 Microenvironmental Concentrations

In the 2009 REA, outdoor microenvironments were identified as contributing appreciably to individual exposure concentrations, and the key area of uncertainty contributing to concentrations for those microenvironments was uncertainty in the ambient air 5-minute concentration estimates. As discussed in section 3.3 above, recent AERMOD improvements might be expected to reduce uncertainty in estimates of 1-hour concentrations across the study area that can vary spatially and temporally. Further, a substantially larger dataset of ambient air measurements is now available that can be used to estimate 5-minute concentrations from 1-hour modeling estimates, for all 12-hour 5-minute periods within each hour (section 3.3.1). Accordingly, reduced uncertainty in estimates of 5-minute ambient air concentrations would be expected to reduce uncertainty in microenvironmental concentrations for both outdoor and indoor microenvironments.

3.4.2 Human Activity Patterns

The time-activity pattern data in CHAD is the basis for the activity sequences simulated by APEX for each modeled individual, including simulation of time spent in different microenvironments, a key influence on individuals' exposure estimates. The CHAD has been significantly updated since its use in the 2009 REA. The database used in the 2009 REA had over 26,000 diaries (including about 12,000 for school-aged children ages 0-18). The CHAD now has over 41,000 diaries, with over 13,000 for school-aged children (U.S. EPA, 2014a). Most of the additional diaries come from more recent studies (2002-2014). This update could reduce the uncertainty in the exposure and associated risk estimates for study populations, including children with asthma.[30]

[30] Although there are some CHAD diaries from persons who have asthma, most do not specify whether or not the individual had asthma. Analyses of the CHAD data that were performed in both the 2009 SO_2 REA (section 8.11.2.2) and the 2014 O_3 REA (U.S EPA 2014b, section 5G-1.4) combined with related findings reported in the extant literature (e.g., van Gent et al. 2007) indicate there is no appreciable difference in the time spent outdoors

3.4.3 Physical Attributes and Ventilation Rate

New information is available in this review for three other inputs to the exposure model. This includes updated NHANES data (2009-2014), which are the basis for the age- and sex-specific body mass distributions from which APEX samples to specify the individuals in the modeled populations. In the uncertainty characterization for the 2009 REA, it was concluded that uncertainty in these data would not affect the exposure estimates in any particular direction and that because random sampling is used, it was expected that the magnitude of influence from this source of uncertainty on exposure estimates would be low (2009 REA, section 8.11.2.2.3).

The other two items considered here are the algorithms used to estimate age-and sex-specific resting metabolic rate (RMR), a key input to estimating a simulated individual's activity specific ventilation rate ($\dot{V}_E$), and the $\dot{V}_E$ algorithm itself. Since the last review, we have been reviewing the literature and evaluating potential updates to the RMR and $\dot{V}_E$ algorithms used in the version of APEX run for the 2009 REA (U.S. EPA, 2008a,b; U.S. EPA, 2009).

With regard to RMR, we have been reviewing the more recent literature and other published sources containing individual data and compiling the associated individual RMR measurements (over 16,000), along with associated influential attributes such as age, sex, and body mass. This comprehensive, diverse collection of data from individuals is being used to develop a new algorithm to replace that used by the version of APEX used for the 2009 REA (version 4.3). That version of APEX used an algorithm for RMR originally based on analyses by Schofield (1985).

With regard to $\dot{V}_E$, new individual measurement data were not found to update the $\dot{V}_E$ database on which the algorithm in the version of APEX used for 2009 REA is based. However, a reanalysis has been performed based on revised assumptions regarding identification of highly influential data points, and with consideration of an additional database variable. This reanalysis is allowing for development of an updated algorithm that utilizes a greater number of samples.

Additional details regarding the RMR and $\dot{V}_E$ data used, algorithm development, and performance evaluation will be available with APEX update, expected in spring 2017. Although each of these expected updates represent improvements to the exposure modeling and reduce uncertainty, the extent to which they might affect resultant estimates is unclear. Note also, the inclusion of these updated data sets and algorithms into the APEX model will be dependent on whether updated model is available as projected in accordance with the current review schedule.

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or exertion levels for individuals with or without asthma. Accordingly, asthma status is not an attribute used in sampling CHAD.

3.4.4 Exposure Estimate Bins

Specific aspects of the approach to binning the estimated exposures to which the E-R functions were applied to estimate risk were recognized to contribute uncertainty to the lung function risk estimates (75 FR 35520, June 22, 2010). For example, the size of the exposure bins carries a certain level of precision, which for exposures generally distributed across a broad range of exposures levels may be acceptable. However, in scenarios assessed in the 2009 REA for air quality conditions associated with potential alternative standards near the existing 1-hour standard, a substantial portion of the exposures fell into very few bins (at the lower end of the range). Thus, for purposes of considering exposures for the existing standard, a greater precision would be desirable particularly at the lowest exposure concentrations. This could be achieved and the uncertainty and any bias contributed by bin size to the risk estimates could be addressed by using smaller-sized bins (e.g., 10 ppb) to represent the exposure estimates.

3.5 CONCLUSIONS

The discussion above reflects the EPA staff assessment of the degree to which currently available information, including that newly available since the last review (e.g., as summarized in the second draft ISA), might be expected to appreciably change our understanding of exposures and risk beyond the insights gained from the assessments from the last review. A critical consideration is the extent to which use of newly available information or approaches in a new or updated quantitative assessment would provide risk estimates for exposure to SO_2 from ambient air that are appreciably different or with which the uncertainty is substantially lower than the estimates generated for the last review. Thus, the decision on whether to develop a comprehensive new assessment of exposure and risk for this review considers the extent to which our characterization of exposure and risk in the last review may remain appropriately informative to the key questions in the current review. Accordingly, it also focuses on the extent to which the newly available information, if applied to aspects of the exposure and risk approach from the last review, has the potential to result in new exposure and risk estimates for which the degree of uncertainty is substantially reduced, or bias is addressed, and that indicates that a new assessment of exposure and risk is warranted to provide an adequate characterization of human exposure and risk, particularly with regard to the existing standard.[31]

Key observations regarding the potential impact of newly available information, particularly focusing on those influencing staff conclusions, are presented here in the general order in which sources of uncertainty are considered in the previous sections.

[31] In considering this point, the EPA staff additionally recognize that such a characterization of exposure and risk, in addition to the currently available evidence, will be considered in the Policy Assessment in terms of both evidence-based considerations and risk/exposure-based considerations.

- *SO_2 Air Concentrations:* There are substantially more 5-minute SO_2 monitoring data available across many more monitors, both hourly maximum 5-minute concentrations and the full series of 5-minute concentrations for each hour, thus providing a substantially improved foundation for estimating 5-minute exposure concentrations that reflect recent information. These new data, in conjunction with improvements to AERMOD since the last review, would also be expected to reduce uncertainties associated with estimating SO_2 concentrations in ambient air across a geographical area. Together this updated information would be expected to substantially improve our characterization of 5-minute SO_2 concentrations in ambient air.
- *Exposure Assessment:* As recognized in section 3.3 above, exposure modeling can be particularly informative to our understanding of the potential for SO_2 concentrations in ambient air to contribute to exposures of concern for at-risk populations (e.g., individuals with asthma while at elevated ventilation rates). A greatly expanded database of activity diaries (CHAD) may be expected to provide a stronger foundation for exposure modeling. In addition, reduced uncertainty in ambient air 5-minute concentration estimates (per above bullet) would be expected to reduce uncertainty in the microenvironment concentrations, including for outdoor microenvironments, which substantially influence peak exposure estimates. Together, this updated information would be expected to contribute to somewhat reduced uncertainty in the exposure estimates.
- *Risk Characterization:* Although little new information is available in this review to characterize lung function response to SO_2 exposures, several steps could be taken to improve upon the lung-function risk model applied in the 2009 REA. Expansion of the dataset that is used to derive lung function E-R functions may reduce uncertainty in the shape of the functions across the study data range. Smaller exposure estimate bins would increase the precision of risk estimates, by better linking estimated exposures with the lung function E-R relationship. Further, sensitivity analyses for the E-R function application to exposures below those studied would augment our characterization of the associated uncertainty contributing to a more robust characterization of lung function risk in the range of the study data and of uncertainties at lower exposures.

With regard to the conceptual model for exposure and health risk, we conclude that the newly available information does not appreciably change key aspects of the conceptual model from the last review. The important new information summarized above would, however, contribute to updated and less uncertain inputs for some aspects of the model (e.g., particularly characterization of 5-minute concentrations), with the potential to be appreciably different from the last review. Such reduction in uncertainty is key aspects of the model would be expected to improve the robustness of the exposure and risk estimates over those from the last review.

We additionally recognize that the 2009 REA did not include an air quality scenario for the current standard of 75 ppb; rather, we relied on inferences drawn from estimates for the air quality scenarios for standard levels bounding the standard (i.e., either just meeting a 50 ppb or 100 ppb standard level). This was the case considering results from both the exposure-based assessment and the air quality-based assessment. The former assessment was essential to our

complete characterization of SO_2-related exposure and associated risk because the air quality-based assessment could not take into account factors that significantly influence actual SO_2 exposures and associated risk, including the movement of individuals through different microenvironments and across large geographic areas all while also at varying breathing rates. Accordingly, in order to adequately consider the exposure/risk implications of the substantially expanded air quality dataset, the exposure modeling-based approach is essential.

In summary, a decision to utilize the new information and approaches summarized above to develop a new REA that provides a more precise characterization of exposure and risk associated with the existing standard, and one with reduced uncertainty, would provide exposure/risk estimates with enhanced utility for informing the current review. Therefore, we conclude that it is appropriate to consider development of an exposure and risk assessment, based on this now available information and methods, to inform the current review of the primary SO_2 standard. Proposed plans for such an assessment are described in chapter 4.

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4 PLAN FOR THE CURRENT HEALTH RISK AND EXPOSURE ASSESSMENT

Based on the newly available data described in Chapter 3, considered along with the existing body of scientific evidence regarding SO_2 exposure and health effects reported in the second draft ISA, we plan to develop a new REA to inform the current review of the primary NAAQS for SO_X. The objective for the REA for this review is to characterize exposure and health risk associated with SO_2 from ambient air under conditions just meeting the current primary standard. The analysis approach for the REA will be based on linking the health effects information to estimated population-based exposures that reflect our improved understanding of 5-minute concentrations of SO_2 in the ambient air (Figure 4-1).

The approach involves estimating human exposures to ambient air-related SO_2 concentrations using a population-based probabilistic exposure modeling approach similar to that performed as part of the 2009 REA (section 4.1). These estimated exposures will be used to evaluate potential health risk using data obtained from controlled human exposure studies, as discussed in section 4.2. To estimate exposure-based health risk, our first approach will rely on a comparison of estimated exposures to benchmark levels of interest (section 4.2.3), while the second will combine exposures with an E-R function to estimate lung function decrements (section 4.2.4). Further, the general approach for how we assess uncertainty and variability in the exposure and risk estimates is summarized in section 4.3. Because APEX uses statistical distributions in describing certain input data and contains conditional probabilities for selection of particular algorithms and personal characteristics, among other stochastic model features, section 4.3.1 provides an overview of how we plan on summarizing the extent to which variability has been accounted for in the exposure and risk assessment. Section 4.3.2 outlines the approach proposed for characterizing uncertainty in the exposure and risk results, considering key uncertainties identified and characterized from the 2009 REA as well as from other NAAQS-related REAs where APEX modeling was performed.

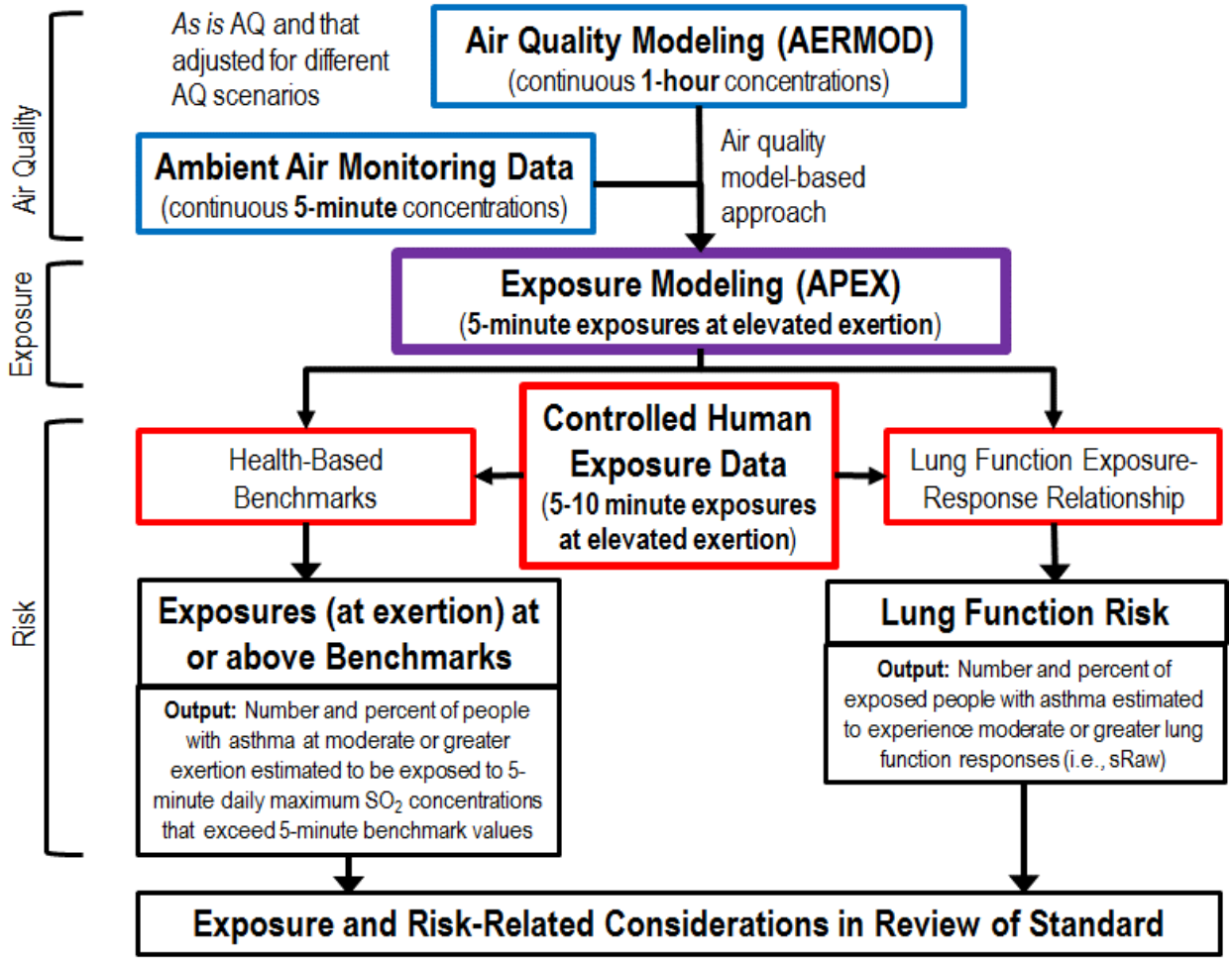

Figure 4-1. Overview of the analysis approach for the REA.

4.1 POPULATION-BASED EXPOSURE ASSESSMENT

Population exposures to SO_2 from ambient air will be estimated for at-risk populations in selected study areas for air quality conditions associated with just meeting the existing primary standard, as well as recent conditions.[32] Exposures will be estimated using the most recent version of the APEX model available.[33] Details regarding the modeling approach, the input data

[32] The need for additional air quality scenarios (if any) will be considered in the draft PA that will accompany the draft REA presenting results for the analyses described here.

[33] Earlier versions of APEX have been used to estimate population exposures to O_3, carbon monoxide, NO_2 and SO_2 in previous NAAQS reviews (U.S. EPA, 2014b, 2010, 2008; 2009 REA) to better inform our understanding of how variability in ambient air pollutant concentrations and other influential attributes relate to human exposure. An APEX model update is expected to be available in spring 2017. The model, associated updated input databases and user's guide will be available at: https://www.epa.gov/fera/human-exposure-modeling-air-pollutants-exposure-model.

to be used, and model specifications for the population groups and study areas of interest are provided in the subsections below.

Because controlled human exposure studies indicate exposures of interest are of short-term duration (5 to 10 minutes), estimated 5-minute average exposures will be the focus in the design of the assessment and in evaluating potential health risk. Potential health risk associated with air quality adjusted to just meet the existing SO_2 standard (and recent unadjusted air quality) will be characterized using two different metrics: (1) the number and percent of the simulated study area population experiencing 5-minute SO_2 exposures at or above benchmark levels of concern (section 4.2.1) and (2) the number of occurrences of lung function decrements (based on predicted occurrence of sRaw increases above 100% and above 200%) in the simulated at-risk populations and the number and percent of the simulated at-risk populations estimated to experience single or multiple occurrences of those lung function decrements (section 4.2.2). Additionally, as part of this analysis, the population-based statistical distribution of exposures will also be evaluated to identify important exposure environments and/or influential activities that lead to those estimated as having greatest potential health risk.

4.1.1 APEX Model Overview

As summarized in section 2.3.2, APEX is a model used to simulate a large number of individuals within a selected study area, that are randomly sampled using a probabilistic approach to reflect the area's population demographics, thus generating study area-wide estimates of population exposure. Any number of simulated individuals can be modeled by APEX, and collectively they represent a random sample of the study area population in the modeled area. Very broadly, APEX stochastically combines information from several large input databases including, but not limited to, the 2010 U.S. Census (e.g., population demographics, home-to-work commuting flows), U.S. EPA's CHAD (e.g., human time-location-daily activity patterns), and temporally-spatially distinct ambient air concentrations. Using these data and several other sources of information, APEX simulates human exposures that occur in user-defined indoor, outdoor, and in-vehicle microenvironments (MEs). Because APEX is capable of using input data at fine temporal (e.g., 5-minute SO_2 concentrations, minute-by-minute human activity patterns) and spatial scales (e.g., census tract SO_2 concentrations) and simulates individuals within a population, the estimated exposures can be output as a time-series of exposures for each and any individual or aggregated to population-based summary exposure metrics of interest. Further details about APEX can be found in the existing Users' Guide and Technical Support Document (U.S. EPA, 2012a, b).

4.1.2 Exposure Domain

The exposure domain is defined by the exposure assessment features of interest, i.e., broadly addressing the questions of where, when, and for whom the assessment pertains. Answers to these questions are informed by the scientific evidence regarding SO_2 exposures and associated health risks, the availability and analysis of the SO_2 concentrations in ambient air at the relevant time scale, reasonableness of technical capabilities (e.g., approach availability and appropriateness), and risk metrics to be generated.

4.1.2.1 Study Areas and Time Periods

We plan to build on the exposure and risk assessments conducted for the last review and continue to focus the assessments on a set of selected study areas. In the 2009 REA, two study areas were evaluated, with each having exposures estimated for a single year. For this REA, we intend to assess exposures in a small number of study areas, each modeled for three consecutive years to evaluate variability in exposures across a 3-year period, consistent with the form of the existing standard.

In considering the available monitoring data with regard to its use in planning and/or performing a REA, we first consider the distribution of monitors in areas across the U.S. and the extent to which a potential study area may be appropriately represented by a single monitor (a single monitor near a specific emission source) or multiple monitors within the study area (e.g., numerous monitors in an urban area). To this end, before developing selection criteria and identifying candidate study areas of interest for modeling exposure and health risk in this REA, we considered the overall local-scale density of the SO_2 monitoring network and developed an approach to define both aggregate and single monitor areas. We first grouped any SO_2 monitors reporting both 1-hour and 5-minute maximum concentrations that were within 10 km of each other, effectively forming a group. Monitors that were not within 10 km of another monitor were considered alone; these single monitor areas represented more than 90% of the SO_2 monitors considered. Using these groupings, we then considered the following factors in the selection of study areas and specific time periods using the following three criteria:

- **Air quality data**: The time period of interest is 2011-2015, because 2011 was the first year having greatly expanded numbers of ambient air monitors reporting 5-minute concentrations and 2015 is the most recent year available to date during the development of this REA Planning Document.[34] A candidate study area needed to have SO_2 ambient air monitoring data that met completeness requirements (section 4.1.4.1) for a recent three-year period, for all three years. This requirement is necessary to calculate design

[34] If 2016 data become available and are in accordance with the REA schedule, they would be included in the study area selection for the REA.

values (next bullet) and to have sufficient data for informing the ambient air concentrations used for exposure modeling. Also, a candidate area needed to have at least one monitor reporting 5-minute SO_2 concentrations.[35] When evaluating available ambient air monitoring data, more than 100 potential study areas met these requirements.

- **Design values**: The design value for the 3-year averaging period in the candidate area should be relatively close to that of the existing standard of 75 ppb. This requirement was designed to minimize the magnitude of the adjustment needed to generate air quality just meeting the existing standard and potentially minimizing the uncertainties in estimates of exposures associated with the adjustment approach. When considering design values ranging from 65 to 85 ppb for any three-year period from 2011 to 2015, 22 candidate areas of the previously identified 100 study areas met this requirement.
- **Population size:** Candidate study areas having the largest populations were given higher priority to better represent at-risk populations. When considering areas having a population of at least 100,000 within 10 km of the centroid of the group of monitors that also met the above design value and air quality completeness criteria, nine candidate study areas remained that met this requirement (see Table 4-1).

For this REA, we considered two approaches to estimating ambient air concentrations for input to the exposure model: a solely monitor-based approach and a model-based approach informed by monitoring data. Both approaches have advantages and disadvantages. For example, an advantage of a monitor-based approach is that, because it uses monitoring data instead of modeling data, uncertainties associated with modeling (e.g. specification of model inputs such as emissions estimates and temporal profiles, meteorology, characterizing building downwash, as well as model selection) would be eliminated. In addition, a monitor-based approach would require fewer resources than a model-based approach. However, a disadvantage of the monitor-based approach is that it may not capture spatially varying SO_2 concentrations across an area, since the approach would assume the monitor measurements reflect the SO_2 concentrations for the area. In addition, a monitor-based approach may limit the exposure domain of the analyses and reduce the size of the population for which exposure could be estimated, though this is dependent on the size of the monitoring network and the area for which it can be judged that the monitors are representative. In contrast to this, an advantage of using a model-based approach is that local-scale concentration gradients may be better represented using a pollutant dispersion technique that accounts for local factors such as terrain and meteorology and a larger exposure domain may be able to be analyzed. Our proposed model-based approach would also be informed by ambient measurements (e.g. data used to approximate 5-minute concentrations from

[35] Study areas having continuous 5-minute data would be preferable to those with only hourly maximum 5-minute data. However, given that there are no monitoring requirements to report continuous 5-minute data at all of the ambient air monitors, we used this as an additional consideration after the initial screening for the top candidate areas.

1-hour modeled data and data used evaluate model performance in predicting spatial variability). However, more resources are needed for the model-based approach and uncertainties associated with the model inputs will need to be considered. That said, for this REA we are proposing to use the model-based approach to estimate ambient air concentrations in each study area, supplemented and informed by available local ambient monitor measurements.

To further refine the above list of these nine candidate study areas, we prioritized areas that have more available SO_2 measurements (i.e. multiple years available of complete data; more than one ambient air monitor in the area; having 5-minute continuous data) that could potentially increase our understanding of the spatial and temporal heterogeneity of ambient air concentrations. Based on this, we identify Brown County, WI, Cuyahoga County, OH, Hillsborough County, FL, and Marion County, IN as potential study areas for assessing exposure and risk based on a number of features. There is diversity in the size and types of potentially influential emission sources (identified as having SO_2 emissions >100 ton per year) in these study areas. Given the configuration of these sources and given their locations with respect to monitor locations, we anticipate the potential for larger temporal and spatial concentration gradients that would not be captured well using monitoring data alone. Accordingly, we believe a model-based approach would be the best choice to estimate ambient air concentrations for input to the exposure model (Figures 4-2 through 4-5).[36] In these areas, the presence of more than one monitor with multiple complete years of SO_2 measurements could increase the degree of confidence in the air quality surface informed by the observed spatial and temporal variability in the ambient monitor data, and ultimately lead to increased confidence in the exposure and assessment results. The modeling domains for these potential study areas would be defined as all possible model receptor points falling within a 10 km radius of the nearby emission sources. When defining the modeling domain for a study area around the emission sources, additional monitors may be included in the group of monitors for the study area beyond those identified in Table 4-1. For example, in Hillsborough County, FL, the initial screening criteria identified a single monitor, but the modeling domain (shown in Figure 4-4) could include two additional monitors in the group.

[36] Because 2014 emissions data for Canadian sources are unavailable at this time, it was determined that including Detroit as a candidate study area would increase the uncertainties associated with a model-based approach.

Table 4-1. Candidate study areas that meet the air quality, design value, and population criteria.

Candidate Study Areas	# of Monitors in Group	DV Monitor in Group	Continuous 5-min Data	2011-2013 DV (ppb)	2012-2014 DV (ppb)	2013-2015 DV (ppb)	Population within 10 km radius	# of Sources in 10 km radius	Source Types
Detroit, Wayne Co., MI	6	261630015	2011-2015	77	72	64	343,201	6	Municipal waste combustor, EGU, steel mill, mineral processing plant
Cleveland, Cuyahoga Co., OH	4	390350038		75	70	62	456,212	4	Steam/heating facility, EGU, steel mill
Marion Co., IN	3	180970057		78	92	79	694,209	4	Lead smelting facility, airport, EGU
Campbell Co., KY (near Cincinnati)	1	210373002		88	72	50	173,127	0	
Green Bay, Brown Co., WI	1	550090005	2013-2015	73	76	75	169,902	5	Pulp and paper, EGU
Hamilton Co., OH (near Cincinnati)	1	390610010		incomplete	67	64	128,195	1	Plastic, resin, rubber product plant
Lemont village, Cook Co., IL	1	170311601		90	66	36	185,764	3	Coke plant, EGU, petroleum refinery
Savannah, Chatham Co., GA	1	130511002		98	78	70	119,776	6	Pulp and paper, pigments, phosphate & fertilizer, EGU, sugar refinery
Tampa, Hillsborough Co., FL	1	120570109	2011-2015	93	79	66	168,867	2	Fertilizer plant, EGU

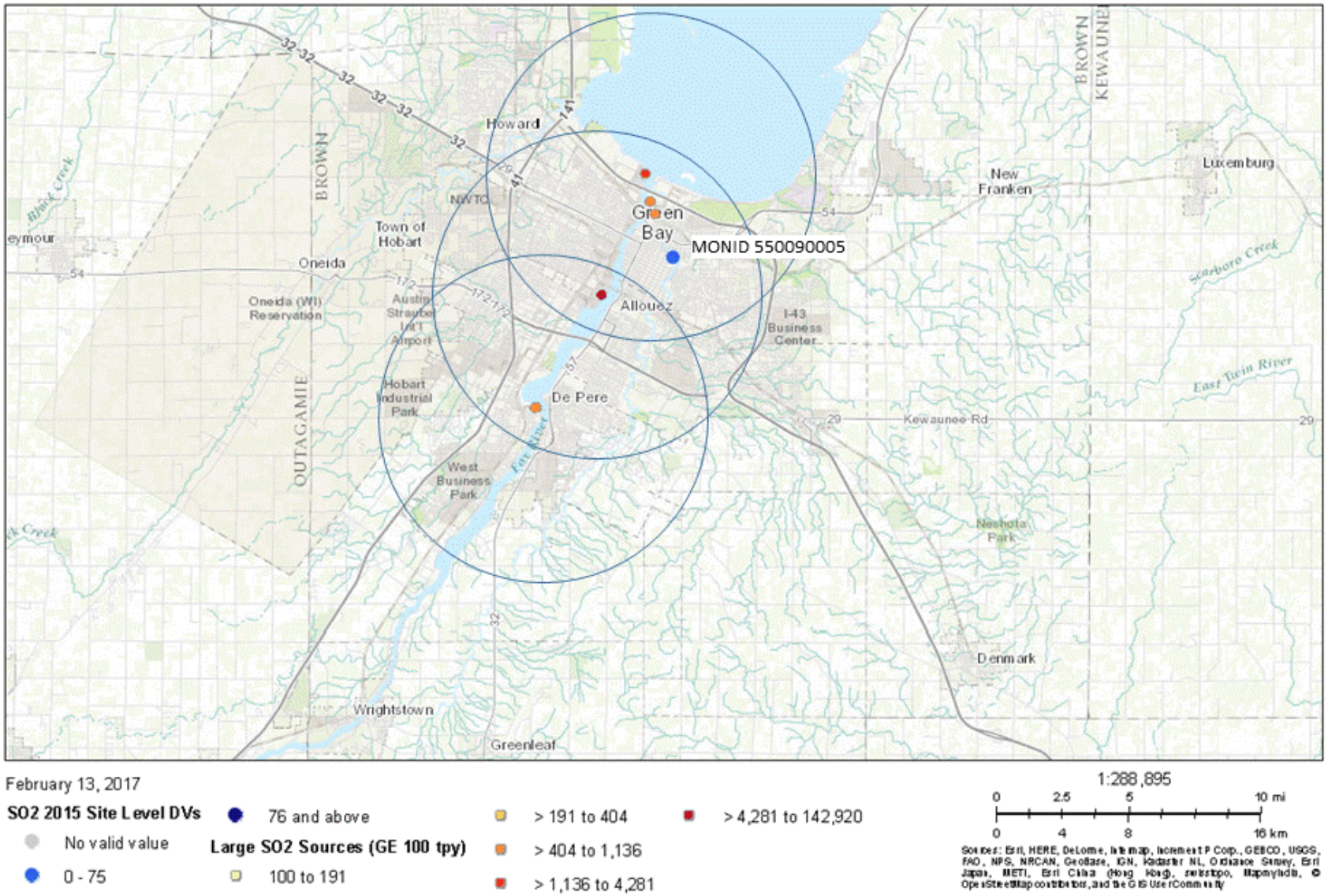

Figure 4-2. Map indicating approximate dimensions of potential model-based study area (blue circles surrounding sources) and SO_2 emission sources > 100 tons per year in Brown County, WI.

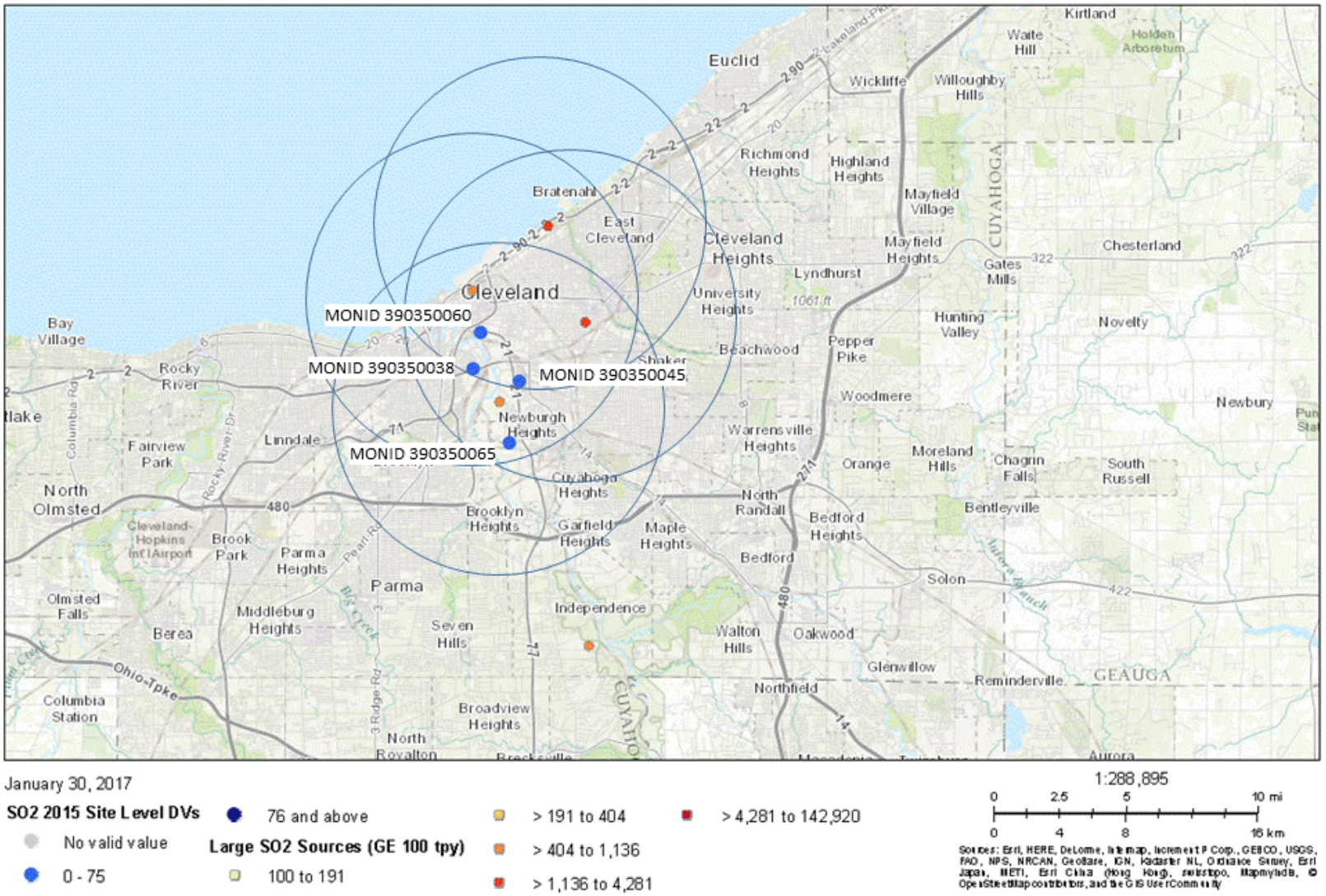

Figure 4-3. Map indicating approximate dimensions of potential model-based study area (blue circles surrounding sources) and SO_2 emission sources > 100 tons per year in Cuyahoga County, OH.

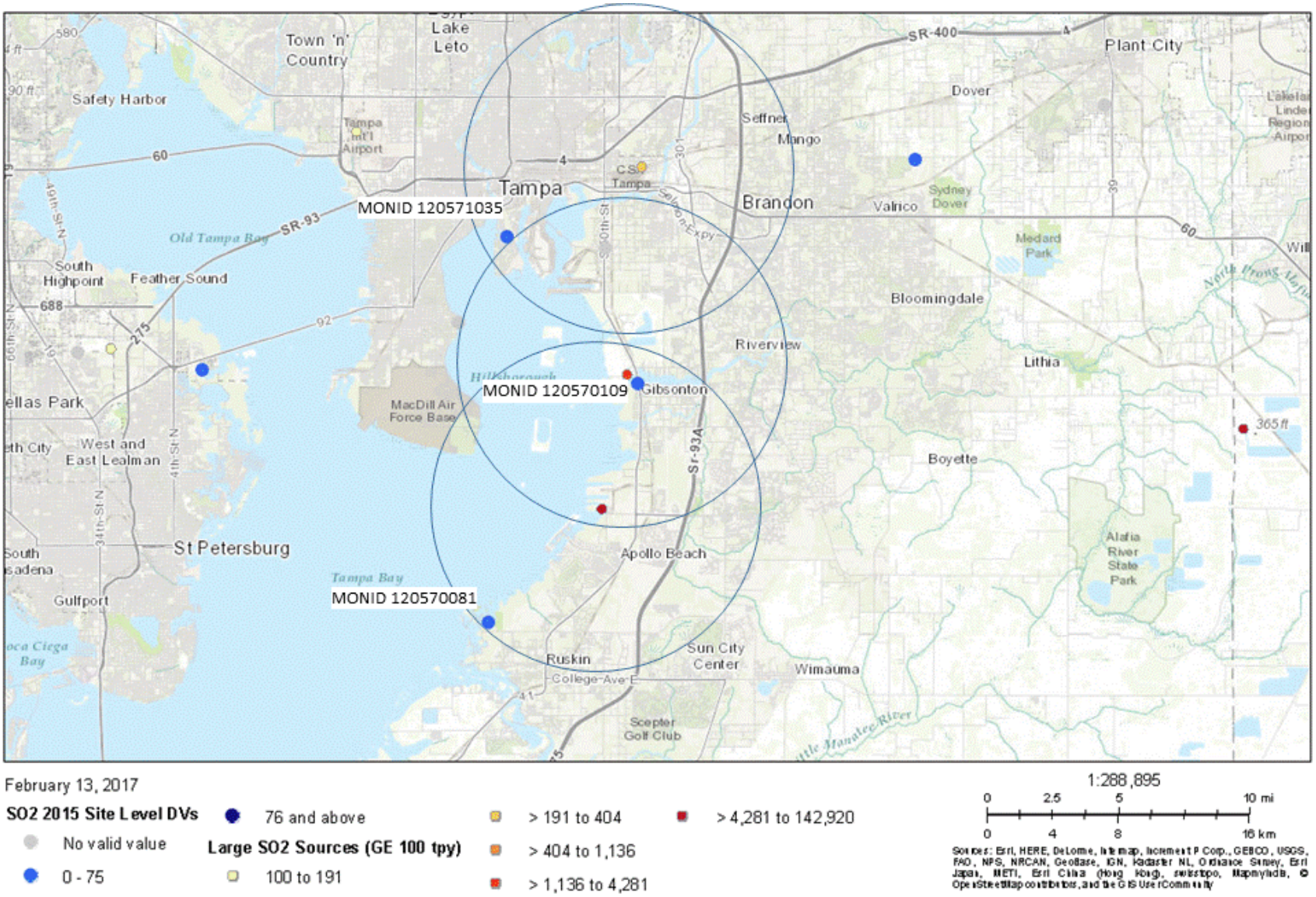

Figure 4-4. Map indicating approximate dimensions of potential model-based study area (blue circles surrounding sources) and SO_2 emission sources > 100 tons per year in Hillsborough County, FL.

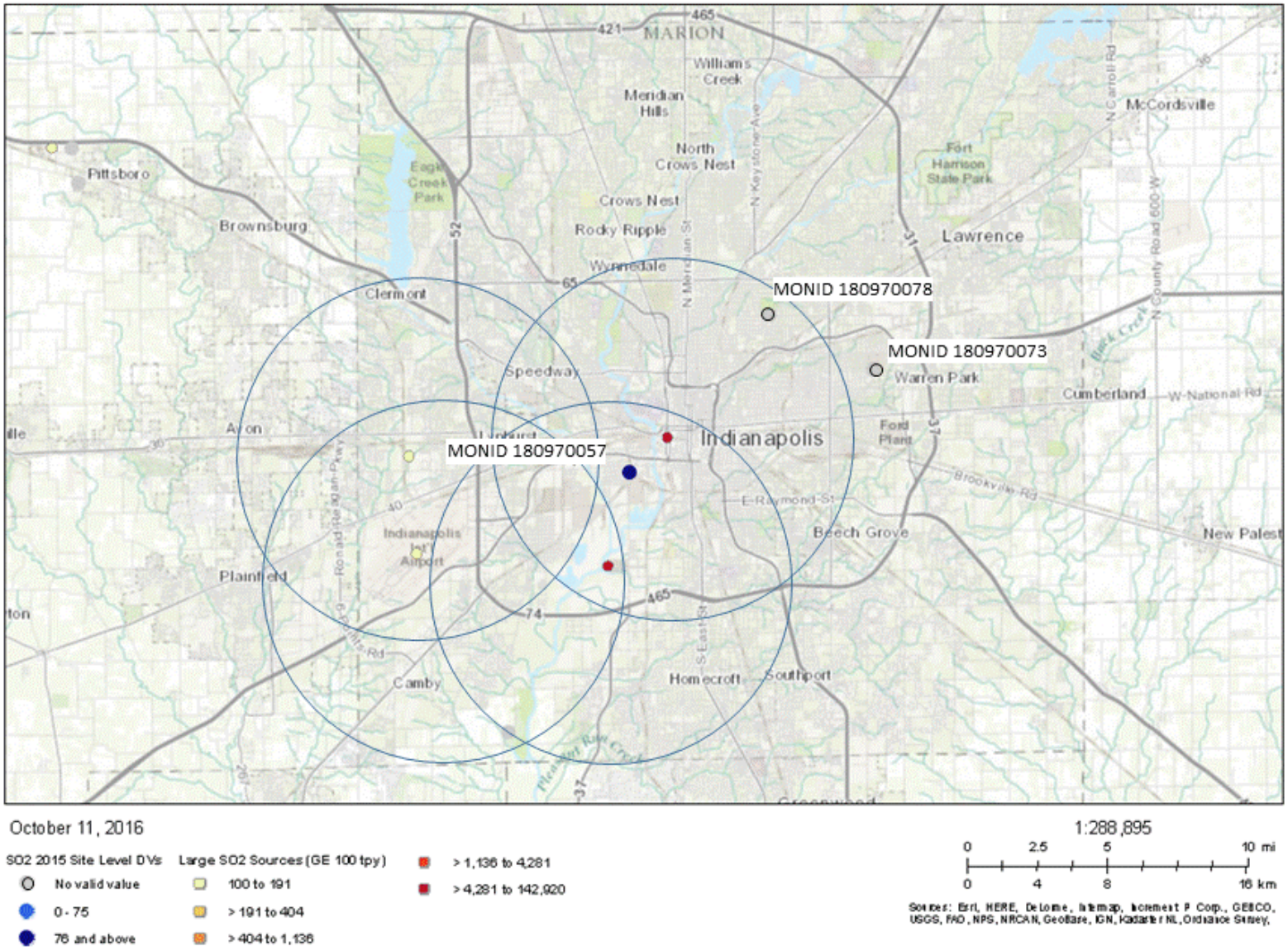

Figure 4-5. Map indicating approximate dimensions of a potential model-based study area (blue circles surrounding sources) and SO2 emission sources > 100 tons per year in Marion County, IN.

4.1.3 SO_2 Concentrations in Ambient Air

Concentrations of SO_2 in ambient air are a key input to APEX in estimating population exposures. The model is fully capable of using a concentration input file having wide ranging spatial and temporal scales. Typically, the complete time-series of hourly ambient air concentrations for a year or season for an urban spatial area is used to estimate exposure concentrations of interest. The temporal scale needed for the air quality is largely based on the temporal scale of the health metric of interest (e.g., 5-minute or 1-hour exposures), while the spatial resolution is largely based on the degree of the spatial heterogeneity in concentrations across the study area. Because the key health effects information is for 5-minute exposures, and thus requiring 5-minute exposure estimates, SO_2 concentrations for ambient air should also be in 5-minute time steps to most appropriately model the exposures of interest.

As described above, we propose to use a model-based approach in the study areas ultimately selected from the candidates listed above. The model-based approach (section 4.1.3.3) to estimate 1-hour ambient air concentrations would rely on emissions estimates and dispersion modeling. This approach would then use information from local 5-minute maximum and/or 5-minute continuous monitor(s) to estimate each hour's time series of 5-minute concentrations at each modeling receptor within the exposure modeling domain. Once this complete time-series of 5-minute data is developed for each receptor point, the ambient concentration data could then be input to APEX to estimate exposures.

4.1.3.1 Monitor Data Completeness Requirements

A requirement for the completeness of monitor data is important when estimating exposures for a full or multiple years. The following steps would be used to determine whether a monitor has a complete year. First a 75% completeness criterion is applied to each day that is monitored; thus, the monitored day would be considered valid if it contains measurements for at least 18 of the 24 hours. Then, the number of days within a quarter of the calendar year are evaluated, also using a 75% completeness criterion. Thus, a monitored quarter would be considered valid if there are at least 68-69 valid days. For a year to be considered complete, all four quarters would need to be valid. In addition, we would also be requiring data for three consecutive years (2011-2013, 2012-2014, or 2013-2015) for the exposure and risk assessments. This criterion is necessary to appropriately calculate the monitor design values relative to the existing primary SO_2 standard.[37]

[37] SO_2 design values are calculated as the 3-year average of the annual 99th percentile of the daily maximum 1-hour average concentrations (appendix T of 40 CFR part 50).

4.1.3.2 Approach for Estimating Missing Values in Ambient Air Monitor Data

Because there will be years when the ambient air monitor did not measure every 1-hour or 5-minute concentration and because APEX needs the complete time-series of 5-minute ambient air concentrations to estimate exposures, an approach is needed to approximate missing values in the ambient air monitor data sets. The goal of the proposed approach is to account for expected variability in ambient concentrations while also recognizing observed temporal (i.e., diurnal and seasonal) patterns in SO_2 concentrations reported in the second draft ISA (sections 2.5.3.2 and 2.5.3.3). The approach is designed to maintain overall characteristics of the measured concentration distribution, remain constrained by the upper bounds of the measurements, and transpose observed temporal variability to the extended air quality surface. The following outlines our proposed steps for estimating missing values for the hourly and 5-minute maximum SO_2 concentrations, considering the 5-year span of ambient air monitoring data (2011-2015).

(1) Normalize the distribution of each reported hourly concentration (either the 1-hour or 5-minute maximum) to the respective annual average concentration, considering each year separately and the complete calendar year of hourly concentrations (e.g., total number of values could be 8,760 for 365 days in year).

(2) Calculate an average distribution of hour-day-month specific factors using measured values, where not missing, and weight by the number of samples in each respective year (thus giving greater influence to monitor-years having the greatest number of samples).

(3) Substitute any hours not having measurements for any year with a value of zero (0).

(4) Calculate the missing concentration in any year by multiplying the hour-day-month specific factor by the annual average concentration for that respective year.

Table 4-2 provides the results of using this approach for data from one monitor in Cuyahoga County, OH (ID 390350038). Reported are several descriptive statistics for the original data along with the extended data having substituted the missing values using the approach described above. By design, there are limited differences in the characteristics of the respective distributions, when comparing the original data set to the substituted data set and considering both the 1-hour concentrations and the 5-minute maximum concentrations. By design, there are no differences in the maximum concentrations for any year. A few patterns emerge, again, resulting from the approach design and indicative of the data set composition. Instances of where ambient air measurements are missing likely occur at times where concentrations are relatively low, thereby yielding slightly lower means and standard deviations when comparing substituted data relative to the unsubstituted data. Consistently, there are small differences when comparing the 95th percentile concentrations, again largely a function of the approach (i.e., most of the substitutions occurred at times when concentrations were expected to be low, thus yielding lower 95th percentile concentrations when replacing missing data).

Table 4-2. Descriptive statistics for evaluating the approach used to substitute missing 1-hour and 5-minute maximum concentrations using a monitor in Cuyahoga County, OH (ID 390350038): all available measurements (no substitution) and that supplemented with data where missing values were present.

Statistic	Year	1-Hour SO_2 Concentrations		Maximum 5-minute SO_2 Concentrations	
		No Substitution	Substituted Missing Values	No Substitution	Substituted Missing Values
mean	2011	4.3	4.2	6.4	6.4
	2012	6.6	6.4	10.0	9.7
	2013	3.9	3.8	5.7	5.6
	2014	4.9	4.9	7.3	7.2
	2015	3.3	3.3	5.1	5.0
standard deviation	2011	7.0	6.7	10.8	10.3
	2012	9.3	8.6	15.0	13.7
	2013	6.1	5.8	9.6	9.1
	2014	7.2	6.2	10.7	9.4
	2015	6.0	5.7	9.8	9.2
minimum	2011	0	0	0	0
	2012	0	0	0	0
	2013	0	0	0	0
	2014	0	0	0	0
	2015	0	0	0	0
median	2011	2	2	3	3
	2012	3	3	4	4.7
	2013	2	2	3	3
	2014	3	3	4	4
	2015	1	1	2	2
p95	2011	16	16	26	25
	2012	26	23	39	35
	2013	15	14	23	22
	2014	18	15.0	27	24
	2015	15	14	23	22
maximum	2011	115	115	173	173
	2012	117	117	206	206
	2013	95	95	136	136
	2014	105	105	132	132
	2015	75	75	180	180
Number of hourly measurements	2011	7606	8760	7606	8760
	2012	6432	8784	6432	8784
	2013	7529	8760	7529	8760
	2014	5433	8760	5433	8760
	2015	7472	8760	7472	8760

To estimate the continuous 5-minute concentrations where only the hourly maximum 5-minute concentrations are reported at all monitors in a study area, we propose the following for where the maximum 5-minute concentration(C_{12}) is less than twice that of the 1-hour average (H):

$$C = \frac{(12 \times H) - C_{12}}{11} \qquad \text{Equation (4-1)}$$

Equation 4-1 assumes the eleven other 5-minute concentrations (C_i, where i = 1, 2,…,11) are the same, and when summed along with the maximum 5-minute concentration and divided by 12 will equal the 1-hour average. For instances where the hourly maximum 5-minute concentration (C_{12}) is ≥ twice the 1-hour average (H), we propose to use a linear ramp generated from the maximum 5-minute concentration as follows:

$$C_i = \frac{(i-1)[(12 \times H) - C_{12}]}{55} \qquad \text{Equation (4-2)}$$

Table 4-3 provides an example of the estimated continuous 5-minute concentrations using this approach for where only the 1-hour average and the maximum 5-minute in a given hour are known. Shown are four hypothetical relationships between the maximum 5-minute concentration and 1-hour average concentration and the resulting estimated concentrations using either Equation 4-1 or Equation 4-2. By design, where the hourly maximum 5-minute concentration is at a level similar to the 1-hour average, all other 5-minute values are also close to the 1-hour value, though less than the reported maximum 5-minute concentration. Where the maximum 5-minute concentration is at least twice that of the 1-hour average, the estimated 5-minute concentrations occurring in that hour progressively decrease below that of the reported maximum 5-minute concentration.

Table 4-3. Example of estimated continuous 5-minute concentrations for hours for which only the maximum 5-minute and 1-hour average concentrations are known and using equation 4-1 or equation 4-2.

Concentration metric	5-minute maximum is			
	< 2 x 1-hour	≥ 2 x 1-hour	≥ 3 x 1-hour	≥ 4 x 1-hour
1-hour average	25	25	25	25
C_{12} (5-min max)	35	50	75	100
C_{11}	24.1	45.5	40.9	36.4
C_{10}	24.1	40.9	36.8	32.7
C_9	24.1	36.4	32.7	29.1
C_8	24.1	31.8	28.6	25.5
C_7	24.1	27.3	24.5	21.8
C_6	24.1	22.7	20.5	18.2
C_5	24.1	18.2	16.4	14.5
C_4	24.1	13.6	12.3	10.9
C_3	24.1	9.1	8.2	7.3
C_2	24.1	4.5	4.1	3.6
C_1	24.1	0	0	0.0
Highlighted cells are where concentrations are known.				

To estimate the complete time series of 5-minute concentrations occurring within an hour using the continuous monitor data, as above, the goal is to maintain the features and bounds of the existing monitoring data. Because there is improved representation of 5-minute concentration variability based on the number of measurements in this data set, a simplified approach is proposed to generate any number of missing values as equivalent to one another while preserving the 1-hour average using the following:

$$C = \frac{[(12 \times H) - \sum_{i=1}^{n} C_i]}{12 - n} \qquad \text{Equation (4-3)}$$

Table 4-4 provides an example of the estimated continuous 5-minute concentrations using this approach for hours for which more than one 5-minute concentration and the 1-hour average concentration are known. Shown are four hypothetical relationships between the maximum 5-minute and 1-hour average concentration and the resulting estimated concentrations using either Equation 4-3.

Table 4-4. Example of estimated continuous 5-minute concentrations for hours for which more than one 5-minute concentration and the 1-hour average concentration are known and using equation 4-3.

Concentration metric	5-minute maximum is			
	≥ 2 x 1-hour	**≥ 2 x 1**-hour	< 2 x 1-hour	< 2 x 1-hour
1-hour average	25	25	25	25
C_{12} (5-min max)	50	50	35	35
C_{11}	40	40	30	30
C_{10}	30	30	25	25
C_9	25	25	20	20
C_8	19.4	20	20	20
C_7	19.4	20	15	15
C_6	19.4	19.2	20.0	15
C_5	19.4	19.2	20.0	15
C_4	19.4	19.2	20.0	22.5
C_3	19.4	19.2	20.0	22.5
C_2	19.4	19.2	20.0	22.5
C_1	19.4	19.2	20.0	22.5
Highlighted cells are where concentrations are known.				

4.1.3.3 AERMOD Predicted Concentrations

We plan to conduct exposure modeling based on AERMOD modeling and informed by SO_2 concentrations measured at ambient air monitors in the study areas and would include model receptor points within 10 km of major sources in the area. As mentioned above, use of a model-based approach can provide perspective on spatial variability in ambient concentrations beyond that represented by only a single or few ambient air monitors in a study area. The monitoring data however provide needed perspective on within-hour temporal variability not captured by AERMOD, because the model is only capable of estimating concentrations as short as 1-hour in duration. Depending on the spatial heterogeneity of SO_2 concentrations within the study areas, the AERMOD receptors could be based on a regularly spaced grid overlaying the study area (e.g., 250 meters) or directly predicted at receptor points linked to exposure modeling population databases (e.g., U.S. Census tracts). The selection of fine-scale receptors is intended to best represent important concentration gradients around the SO_2 emission sources, though modeling efficiency is also an important consideration. We anticipate performing preliminary model runs surrounding sources to determine the scale that best captures concentration gradients, while also preserving some degree of practicality (e.g., input/output file sizes and APEX model simulation run times compared with concentration heterogeneity gained/lost).

Input emissions will either be: (1) hourly emissions for those sources with hourly data (e.g., EGUs), or (2) temporally varying emissions for non-hourly sources using recommendations in the SO_2 Modeling Technical Assistance Document (SO_2 MTAD) developed for the SO_2 Data Requirements Rule and designations process (U.S. EPA, 2016). The recommendations outlined in the SO_2 MTAD discuss how to format hourly emissions for AERMOD and how to calculate temporally varying emissions for non-hourly sources using annual emissions, throughput (e.g. tons of coal used per month, season, etc.) and operating schedules. Other aspects of the modeling (meteorological data, etc.) will follow recommendations in the SO_2 MTAD and the *Guideline on Air Quality Modeling* (Appendix W of 40 CFR Part 51). Model performance (e.g., comparison with available monitor data) can be evaluated using procedures outlined in the EPA Protocol for Determining Best Performing Model (U.S. EPA, 1992). Surface meteorological observations will be obtained from the National Climatic Data Center[38] to provide hourly data for input to AERMOD and APEX, using meteorological stations within or near each selected study area.

For the SO_2 exposure assessment, we would need to estimate 5-minute values from the AERMOD hourly concentrations. We plan to use information from 5-minute concentrations obtained from the monitoring data maintained in EPA's Air Quality System (AQS).[39] For each hourly concentration at each AERMOD receptor location, we plan to estimate the corresponding twelve 5-minute values within that hour. Our proposed approach for estimating 5-minute SO_2 concentrations from hourly AERMOD predictions is to replicate the pattern of the monitored 5-minute values in an hour by scaling the 5-minute values so their hourly averages are equal to the AERMOD predictions for that hour (Equation 4-4).

$$Y_{shi} = \frac{Y_{sh}}{\frac{1}{12}\sum_{i=1}^{12} X_{hi}} X_{hi}$$

Equation 4-4

where

X_{hi} = the ith 5-minute value during hour h at the monitor,
Y_{sh} = the AERMOD value at location s, hour h,
Y_{shi} = the ith 5-minute value during hour h, at location s,
s = AERMOD prediction point in space,
h = hour of day
i = sequence of 5-minute values within the hour, i=1, 2,..., 12.

[38] See http://www.ncdc.noaa.gov/oa/ncdc.html

[39] http://aqsdr1.epa.gov/aqsweb/aqstmp/airdata/download_files.html

Thus, we plan to use the complete calendar year of continuous 5-minute concentrations and to apply that same concentration variability to the AERMOD receptor, using the complete time-series of hourly scaling factors (unique to each receptor), to yield the time series of 5-minute SO_2 concentrations (e.g., n= 12*24*365 = 105,120 values) at every receptor in the exposure modeling domain. Effectively, all spatial gradients that may exist within each hour across the study area are maintained, the 5-minute monitoring data are adding a finer scale to the within hour temporal variability. For study areas having only one ambient monitor available to inform the estimation of 5-minute concentrations, because the within hour temporal variability will also be maintained (i.e., the 5-minute pattern for the entire year is guided by one monitor), the spatial gradient across all receptors will also be preserved for every 5-minute concentration. For instances where a study area has more than one monitor, we propose that the hourly concentrations predicted at the AERMOD receptors use data from the nearest monitor having 5-minute concentrations. Again, all spatial gradients that may exist within each hour across the study area are maintained. However, because there is more than one 5-minute pattern to draw from and use to generate within hour temporal variability, it is possible that the spatial gradients observed for the 1-hour do not exactly match the gradients estimated for 5-minute concentrations. The occurrence of this will likely be limited to a fraction of receptors and during a limited number of 5-minute periods. The occurrence of this is considered acceptable because the intent of the overall approach in linking information from both the model and the monitors is to better inform the air quality surface by using the best of what each approach has to offer.

4.1.3.4 Adjusting Concentrations to Just Meet a Standard

The exposure and risk analyses will be conducted for air quality adjusted to just meet the existing primary SO_2 standard, as well as for recent (unadjusted) air quality. As described in Chapter 2, a proportional adjustment approach was used in the 2009 REA. An analysis at that time demonstrated that proportional adjustment is an appropriate approach (Rizzo, 2009). We have analyzed recent air quality data to evaluate this assumption for purposes of the planned REA. Focusing on the monitor in each study area having the highest design value during the 2011-2015 period, we compared the monitoring data for a low concentration year with data for a high concentration year, with low and high defined by having a design value that is either below (a low year) or above (a high year) the level of the existing standard (99th percentile daily maximum 1-hour of 75 ppb). Figure 4-6 shows the results for each of the four potential study areas for monitors having the highest design values, with plots for each of the other monitors shown in Appendix C.

The results of these new comparisons are similar to what was observed previously (Rizzo, 2009). In some study areas and at some monitors, there is linearity or proportionality

when comparing high year to low year concentrations, indicating that adjustments made using a uniform factor is an acceptable approach to estimating alternative air quality scenarios (e.g., Cleveland County, OH; Brown County, WI). Occasionally, there are features of the concentration distribution that do not entirely reflect a linear/proportional relationship, including curvilinear features, non-zero regression intercepts, and upper percentile concentrations both above and below the linear regression line (e.g., Marion County, IN). Given that the adjustment for the ambient air concentrations considered in the exposure assessment are likely to be small (< 10%, Table 4-1), the impact of deviations from proportionality is also likely to be limited. Thus, based on these analyses, we plan to use the same proportional adjustment approach in the REA for the current review as had been used in the 2009 REA, although instances where the potential impact may be greatest will be evaluated (e.g., in Marion County, IN).

Before adjusting air quality to just meet a standard of interest, typically a design value (DV) is calculated for locations in the study area. When using a proportional adjustment approach, the highest DV is used to derive a single multiplicative factor (*F*) to adjust the monitored concentrations across the study area. For the planned REA for the current review, in each study area, *F* will be calculated by dividing 75 ppb by the DV and will be used to adjust all SO_2 concentrations in a study area by this factor to simulate just meeting the existing standard. Note, this adjustment of air quality will be based on three years of concentrations, consistent with the form for the existing standard. For each study area, we will have both a predicted air quality surface from AERMOD and measurement data from one or more ambient monitors. Determination of the most appropriate design value to use for adjusting ambient concentrations in each study area will depend on comparisons of the predicted receptor concentrations with the monitoring concentrations. Based on this assessment, the adjustment factor(s) selected, descriptions for how they were derived, and their application will be provided in the REA.

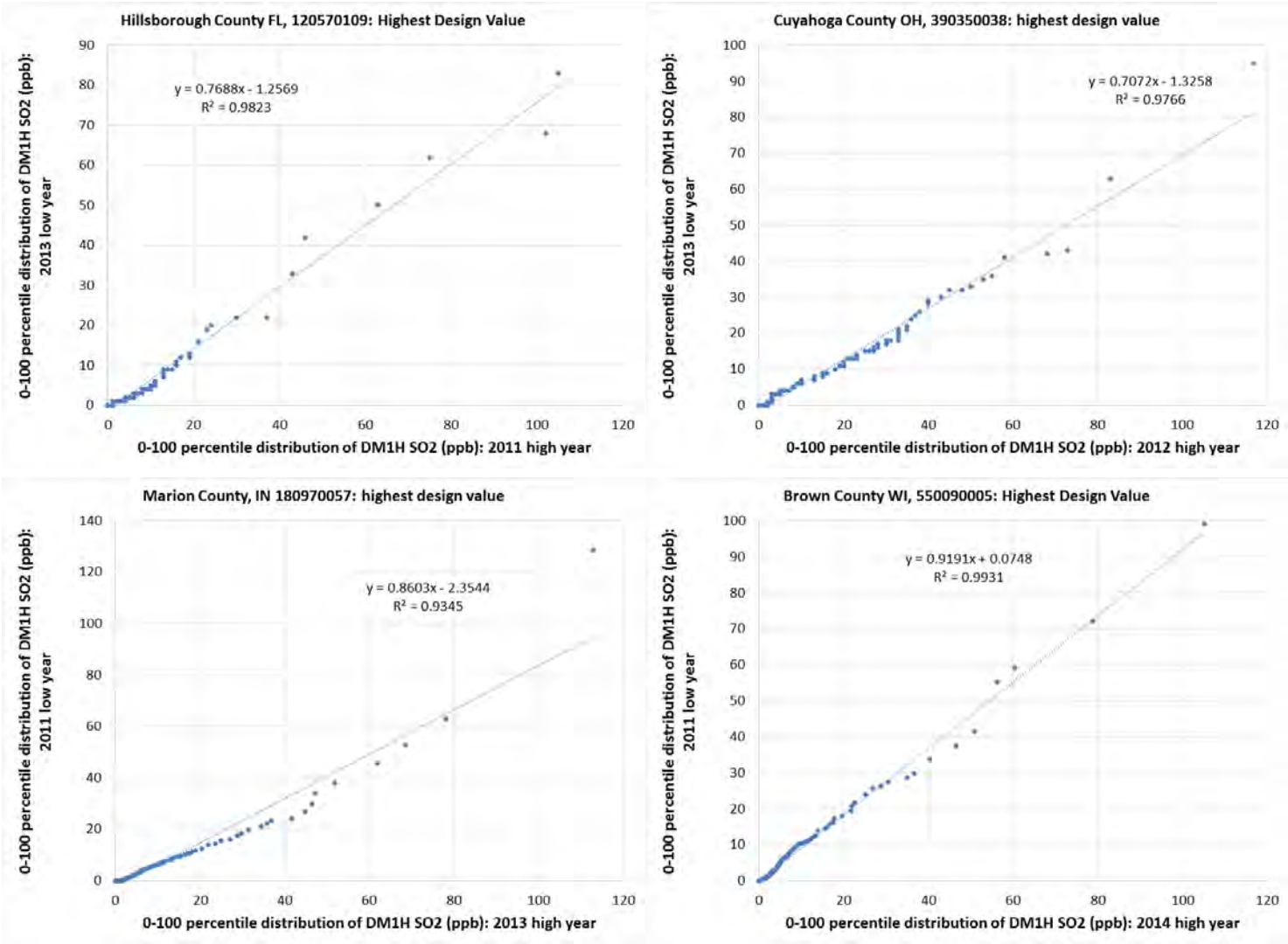

Figure 4-6. Comparison of low and high concentration years using recent data (2011-2015) for daily maximum 1-hour SO_2 concentrations in ambient air in Hillsborough County, FL (top left), Cuyahoga County, OH (top right), and Marion County, IN (bottom left), and Brown County, WI (bottom right).

4.1.4 Microenvironmental Concentrations

The SO_2 concentrations in each microenvironment (ME) will be estimated using either a mass-balance or a factors approach, and the user specifies the probability distributions of the parameters used for the concentration calculations (e.g., indoor-outdoor air exchange rates). These distributions can flexibly depend on the values of other variables in the model. For example, the distribution of air exchange rates in a home, office, or car depends on the type of heating and air conditioning present, which are also stochastic inputs to the model. The user can choose to retain the value of a stochastic parameter constant for the entire simulation (e.g., house volume would remain the same throughout the exposure period), or can specify that a new value shall be sampled hourly, daily, or seasonally from specified distributions. APEX also allows the user to specify diurnal, weekly, or seasonal patterns for certain ME parameters.

The calculation of ME concentrations in APEX is dependent not only on the parameter distributions for the mass balance and factors approaches, but also on the ambient (outdoor) air SO_2 concentrations and temperatures. In the 2009 REA, twelve MEs were used to estimate exposures. In considering the 2009 REA results showing that the majority of peak SO_2 exposures occur outdoors (2009 REA, Figure 8-21) and recognizing the similarity of the focus of the 2009 REA with that of the current REA (i.e., understanding short-term peak exposures), identifying and distinguishing this number of MEs is unnecessary. We propose to aggregate the number of MEs, still proposing a core mix that addresses exposures of ambient origin that occur within indoor, outdoor, and vehicle MEs. For this application to SO_2, the following five MEs will be modeled:

- Indoors - residence
- Indoors - all other (e.g., offices, shopping)
- Outdoors - all other (e.g., residence, public parks)
- Outdoors - near-road (e.g., near-road, public garage)
- In vehicles (e.g. automobile, bus)

Parameters defining each microenvironment will be specified by distributions that reflect the variability of these parameters. The parameters used depend on whether a microenvironment is modeled using the factor-based model or the mass balance model. We will not be modeling indoor sources of SO_2 in this analysis, because our focus is on exposure to SO_2 of ambient air origin.[40] We still expect the outdoor MEs to be the most important regarding peak 5-minute SO_2

[40] Indoor SO_2 sources can include secondary heating sources (e.g., fireplaces, space heaters), however, personal SO_2 exposure measurements have generally been lower than ambient air concentrations, indicating personal exposure to generally be dominated by ambient air exposure (2008 ISA, section 2.6.3; second draft ISA, section 3.4.1).

exposures, based on a finding in the 2009 SO_2 REA indicating peak exposures occurred much more frequently in outdoor MEs than within indoor and vehicle MEs (second draft ISA, p. 3-23).

We plan to use a factor-based model to simulate the outdoors and outdoors near-road MEs, for which the mass-balance model is not applicable, and also the in-vehicles ME, for which adequate data are not available to use the mass-balance model. Two parameters affect the pollutant concentration calculation in the factors method, the proximity and infiltration factors. The proximity factor ($\boldsymbol{F}_{PR}$) is a unitless parameter that represents the relationship of the ambient air concentration outside of the ME ($\boldsymbol{C}_O$) to the concentration at a monitoring station ($\boldsymbol{C}_A$) by the equation $\boldsymbol{C}_O = \boldsymbol{F}_{PR}\,\boldsymbol{C}_A$. The infiltration factor ($\boldsymbol{F}_{inf}$) is a unitless parameter that represents the equilibrium fraction of pollutant entering a ME from outside the ME. The concentration inside the ME ($\boldsymbol{C}_I$) is estimated by the equation $\boldsymbol{C}_I = \boldsymbol{F}_{inf}\,\boldsymbol{C}_O$. The infiltration factor in the factor-based model is often expressed as:

$$\boldsymbol{F}_{\text{inf}} = \frac{\boldsymbol{Pa}}{\boldsymbol{a}+\boldsymbol{k}}$$

where $\boldsymbol{P}$ is a penetration coefficient, $\boldsymbol{a}$ is an air exchange rate, and $\boldsymbol{k}$ is a loss rate. APEX draws values of these parameters from ME-specific distributions specified by the user, to model the stochastic nature of these factors. In a practical sense, the infiltration factor for modeling outdoor MEs are assumed equal to 1.

The mass balance model is more appropriate for complex MEs and where data are available to model such MEs. We plan to use the mass balance model for the indoor MEs. The mass balance model assumes that an enclosed ME (e.g., a room in a residence) is a single well-mixed volume in which the air concentration is approximately spatially uniform. APEX estimates the concentration of an air pollutant in such a ME by using the following three processes:

- Inflow of air into the ME
- Outflow of air from the ME
- Removal of a pollutant from the ME due to deposition, filtration, and chemical degradation

In addition to proximity factors, the mass balance model supports parameter distributions for time varying emissions sources, decay rate, air exchange rate, volume, and removal rate. We plan to estimate the distributions of these ME-specific parameters based on existing data used for 2009 REA and other recent REAs (e.g., the 2014 O_3 REA) and update these parameters using any newly available information, where appropriate. The description of the final ME-specific parameters, their sources of information, and an assessment of representativeness will be provided in the REA.

4.1.5 At-Risk Populations

The second draft ISA identifies people with asthma to be at increased risk of respiratory-related effects associated with short-term peak SO_2 exposures (second draft ISA, Table 6-7 and section 6.3.1).[41] As discussed in section 4.2 below, controlled human exposure studies support this conclusion and provide information on exposure duration and concentrations associated with effects in people with asthma. In addition to characterizing exposure and risk for adults with asthma, we will also develop separate exposure and risk estimates for school-aged children (ages 5-18) with asthma, as the evidence indicates that children with asthma may be at increased risk compared to adults with asthma. Children under the age of 5 will not be included in this assessment because the CHAD database has relatively fewer activity patterns in the database to represent that population group[42] compared with those for school-age children and that there may be greater uncertainty in estimating important physiological attributes (e.g., their activity specific METs). Use of this age group is consistent with REAs performed for other NAAQS pollutants (e.g., 2014 O_3 REA, 2010 NO_2 REA).

4.1.6 Simulated Individuals

As summarized in section 2.3.2.2, APEX stochastically generates a user-specified number of simulated persons to represent the population in the study area. The number of simulated individuals can vary and depends on the size of the population to be represented, though we expect the number of simulated individuals to be about 50,000 – 100,000. Each simulated person is represented by a "personal profile." The personal profile includes characteristics such as a specific age, a specific home sector, a specific work sector (or does not work), specific housing characteristics, specific physiological parameters, and so on. The profile does not correspond to any particular individual in the study area, but rather represents a simulated person. While a single profile does not have much meaning in isolation, a collection of profiles represents a random sample drawn from the study area population. This means that statistical properties of the collection of profiles should reflect statistical properties of the actual population in the study area.

As summarized in section 2.3.2, APEX generates population-based exposures through the use of several population databases. Based on the defined study area and study groups, APEX will simulate representative individuals using appropriate geographic, demographic, and health

[41] There are several other population groups evaluated in the second draft ISA, however only people with asthma were considered as having adequate evidence for potential increased SO_2 exposure and increased risk of SO_2-related health effects (second draft ISA, section 6.6).

[42] Based on the most recent CHAD database, the limited amount of activity pattern information mainly affects diaries for children aged 0 to < 2 years old.

status information provided by existing population-based surveys. APEX generates the simulated person or profile by probabilistically selecting values for a set of profile variables such as demographic variables, which are defined by the 2010 U.S. Census data, personal and physiologic attributes (described below), and other modeling variables.

Once the immediate demographic variables are identified by APEX for a simulated individual in the study area, the other variable values are selected as well as the development of the activity patterns that account for the places the simulated individual visits and the activities they perform. The following subsections describe the population data we plan to use in the assessment to assign key features of the simulated individuals, and approaches used to simulate the basic physiological functions important to the exposure estimates for this REA.

4.1.6.1 Population Demographic Information

To stochastically simulate the population of interest, APEX will use probability distributions derived from the 2010 Census. In the past, we have most commonly done this at a census tract level, though it is possible to do so at the block-level. Determination of the most appropriate spatial scale to use will be based on evaluations of the spatial heterogeneity in SO_2 concentrations in the selected study areas (section 4.1.3.3) and a practical consideration of the anticipated impact to exposures of finer-scale modeling weighed against the resources needed to perform the modeling at that scale. Regardless, we plan to use population counts from the 2010 Census of Population and Housing Summary File 1.[43] Summary File 1 (SF 1) contains what the Census program calls "the 100-percent data," which is the information compiled from the questions asked of all (100% of) people and housing units in the U.S.

In the 2010 U.S. Census, estimates of employment were developed by census tract and will be used in the REA. The file input to APEX will be broken down by sex and age group, so that each sex/age group combination is given an employment probability fraction (ranging from zero to one) within each census tract. The age groupings in this file currently are: 16-19, 20-21, 22-24, 25-29, 30-34, 35-44, 45-54, 55-59, 60-61, 62-64, 65-69, 70-74, and greater than 75 years of age. Because there is no employment information for children under 16 years of age, simulated individuals in that age group are assumed to be unemployed and will be given an employment probability fraction of zero.

4.1.6.2 Asthma Prevalence

In previous REAs for which people with asthma are a simulated at-risk population, we have attempted to account for common factors that are known to influence observed asthma

[43] Technical documentation - 2010 Census Summary File 1—Technical Documentation/prepared by the U.S. Census Bureau, Revised 2012 - available at: http://www.census.gov/prod/cen2010/doc/sf1.pdf.

prevalence, such as age, sex, and U.S region. In better accounting for these factors, we could better represent the estimated exposures that these potentially at-risk population groups might experience. For the 2014 O_3 REA in particular, we expanded the list of potential influential factors to not only address person-level attributes but to also include a more specific geographic-level attribute to better link the potentially at-risk population group(s) to spatially heterogeneous ambient concentrations. This was motivated by observations that (1) there are notable differences in asthma prevalence by age, gender, region, and poverty status, (2) there is variability in the spatial distribution of poverty status across census tracts, stratified by age, and (3) there is spatial variability in local scale ambient concentrations of many air pollutants, we developed a database that provides estimates of asthma prevalence at a census tract level (2014 O_3 REA, Appendix C).

We have updated the previously used database to include recent demographic information obtained from the U.S. Census for use in this current REA.[44] The same asthma prevalence (2006-2010) was included, originally obtained from the Center for Disease Control (CDC) and Prevention's National Health Interview Survey (NHIS).[45] The asthma prevalence was stratified by NHIS defined regions (Midwest, Northeast, South, and West), sex, age (single years for ages 0-17) or age groups (ages ≥ 18), and by a family income/poverty ratio.[46] Asthma prevalence was then linked to U.S. census tract level poverty ratio probabilities, also stratified by age and age groups, to generate a final database consisting of census tract level asthma prevalence for the entire U.S. A summary of the asthma prevalence approximated for each potential study area is provided in Table 4-5. The updated database containing asthma prevalence stratified by age (or age groups) and sex for each tract in the selected study areas will be provided as part of the REA.

[44] Summary tables (B17024) used from the 5-year American Community Survey data for 2008-2012 are available at: https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?src=bkmk

[45] See http://www.cdc.gov/nchs/nhis.htm (accessed October 4, 2011).

[46] The income/poverty ratio threshold used was 1.5, that is the surveyed person's family income was considered either ≤ or > than a factor of 1.5 of the US Census estimate of poverty level for the given year.

Table 4-5. Estimated asthma prevalence for children and adults in four potential study areas.

Study Area (# tracts)	Study group	Asthma Prevalence (in percent of population)		
		mean	minimum	maximum
Brown Co., WI (54)	child	11.1%	9.8%	13.6%
	adult	7.9%	6.4%	9.3%
Cuyahoga Co., OH (443)	child	11.9%	9.4%	16.0%
	adult	8.4%	7.0%	12.4%
Hillsborough Co., FL (316)	child	10.5%	8.7%	13.1%
	adult	6.8%	6.0%	8.9%
Marion Co., IN (224)	child	12.0%	9.0%	15.0%
	adult	8.4%	7.2%	10.4%

Based on combining information from CDC NHIS asthma prevalence and US census income/poverty ratios. Prevalence statistics in this table are based on tract-level summaries within each county that were generated by aggregating age (or age group), and sex specific prevalence estimates, and weighted by each age/sex specific population. The mean is average of all tracts, the minimum is the lowest prevalence in a tract, the maximum is the highest prevalence in a tract, within each the county.

4.1.6.3 Commuting

The commuting patterns of the study area's employed individuals will be simulated at the census tract level using a national commuting database in conjunction with estimates of employment by tract. This allows APEX to approximate home-to-work commuting flows between census tracts. We plan to use the national commuting database provided with APEX in this analysis. Commuting data were derived from the 2010 Census and were collected as part of the U.S. DOT Census Transportation Planning Package.[47] The data used to generate APEX inputs are from the "Part 3-The Journey To Work" files. These files contain counts of individuals commuting from home to work locations at a number of geographic scales. These data have been processed to calculate fractions for each tract-to-tract flow to create the national commuting data distributed with APEX. This database[48] contains commuting data for each of the 50 states and Washington, D.C. This data set does not differentiate people that work at home from those that commute within their home tract.

4.1.6.4 Human Activity Patterns

As in the 2009 REA, APEX will draw on CHAD (McCurdy et al., 2000), most recently updated by U.S. EPA (2014a) for longitudinal activity sequences, representing the movement of

[47] These data are available from the U.S. DOT Bureau of Transportation Statistics at the web site: http://transtats.bts.gov/.

[48] The most recent version of this database is available as part of the input and output files associated with the 2014 O_3 REA and can be downloaded from https://www.epa.gov/fera/download-trimexpo-inhalation-apex.

simulated individuals through time and space.[49] The locations used in the CHAD diaries are assigned to the specified APEX MEs.[50] For each event[51] in an individual's activity pattern, APEX calculates the concentration in the associated ME (see section 4.1.4 above). The model then combines the event-specific exposures to obtain a continuous time-series of exposures spanning the time period of interest. For SO_2, as summarized in section 2.3.2 above, it is important to have an understanding of exertion levels associated with each activity. CHAD contains statistical distributions of activity-specific METs developed from literature-derived data, which are used to estimate the energy expended (and associated breathing rates) while an individual performs particular activities. Further details regarding the METs distributions and related physiological algorithms used in the current version of APEX are provided in U.S. EPA (2012b).

Further, when performing multiday simulations, an approach is needed to generate the longitudinal series of diary days for each simulated individual because most of the diary data in CHAD are cross-sectional, i.e., the information that originated from the surveyed individual captured only a single or few consecutive days of their activity patterns. To overcome this limitation, APEX provides three methods of assembling composite diaries. The first (basic) method, which is adequate for estimating mean exposures, simply involves randomly selecting an appropriate activity diary for the simulated individual from the available diary pool. The second method is a more complex algorithm for assembling longitudinal diaries that realistically simulates day-to-day (within-person correlations) and between-person variation in activity patterns (and thus exposures). The third method uses a Markov-chain clustering algorithm to also recreate realistic patterns of day-to-day variability.

For this application we plan to use the second approach to capture the tendency of individuals to repeat activities, based on reproducing realistic variation in a key diary variable (Glen et al., 2008). For this SO_2 exposure and risk assessment, the key variable selected is the amount of time an individual spends outdoors each day, one of the most important determinants of exposure to high levels of SO_2 (second draft ISA, section 3.4.1). This longitudinal method

[49] The sequences generated by CHAD account for factors such as particular day-types (e.g., weekday versus weekend) and outdoor temperature, and how they influence daily activities and peoples' exposures. The data contained within CHAD come from multiple surveys with varied structures, though in general, the surveys have a central commonality based on their containing daily diaries of human activity information. Relevant demographic attributes of these individuals, such as age and sex, are included as well.

[50] There are many more CHAD locations than MEs being modeled (there are over 100 CHAD locations and five MEs to be modeled in this assessment). Thus, most of the MEs will have multiple CHAD locations mapped to them.

[51] Exposure events are when an individual is in a single microenvironment, exposed to a constant concentration for a specific duration of time, and while at a constant activity level. The duration of the event is a maximum of 1 hour due to the structure of the time-location-activity diary, but could be as short as 1 minute.

targets two statistics, a population diversity statistic (D) and a within-person autocorrelation statistic (A). Values of 0.2 for D and 0.2 for A were initially developed based on analyses by Geyh et al. (2000) and Xue et al. (2004), with both studies evaluating groups of children ages 7 to 12 in a single study area. We may adjust values for D upwards to 0.5 to reflect a broader range of ages and to better estimate repeated activities. Further details regarding the development of the longitudinal methodology can be found in U.S. EPA (2012b).

4.1.6.5 Personal Attributes

In addition to the above demographic information in constructing simulated individuals, each modeled person can be assigned status and personal attributes. All of these variables are treated probabilistically in APEX, taking into account interdependencies where possible, and reflecting variability in the population. The EPA regularly makes improvements to APEX. If additional updates regarding new approaches or data are completed in time for use in the REA for this review, then these updates will be fully described in the new REA.

4.1.6.5.1 Status Attributes

Status variables are factors deemed important in estimating ME concentrations, and can include, but are not limited to, people's housing type, whether their home has air conditioning, and whether their car has air conditioning. Because outdoor MEs are expected to contribute the most to an individuals' highest exposure (and potential health risk) and these factors largely pertain to indoor MEs, further details regarding these will be provided in the REA.

4.1.6.5.2 Physical Attributes

Personal attributes can be important when estimating pollutant specific dose and can include height, weight, and body surface area. Two key personal attributes determined for each individual in this assessment are body mass and BSA. Each simulated individual's body mass is randomly sampled from recently updated age- and sex-specific body mass distributions and generated from NHANES data for the years 2009-2014.[52] Then age- and sex-specific body surface area can be estimated for each simulated individual.

4.1.6.5.3 Ventilation Rate

Human activities are variable over time, and a wide range of activities are possible even within a single hour of the day. The type of activity an individual performs, such as sleeping or jogging, will influence their ventilation rate. APEX estimates minute-by-minute ventilation rates that account for the expected variability in the activities performed by simulated individuals. The second draft ISA indicates that the lung function responses associated with short-term peak SO_2

[52] Original data are available at https://wwwn.cdc.gov/nchs/nhanes/Default.aspx. Actual distributions used will be part of the APEX input/output file package generated for this REA.

exposures coincide with moderate or greater exertion (second draft ISA, section 5.2.1.2). In our exposure modeling approach, we will use APEX to generate the complete time series of activity-specific ventilation rates and the corresponding time-series of estimated SO_2 exposures. APEX will then aggregate both the ventilation rate and exposure concentration to the averaging time of interest (a 5-minute average). Thus, the model will provide exposure estimates for the simulated individuals that pertain to specific target levels for both ventilation rate and exposure concentration. The approach to estimating activity-specific energy expenditure and associated ventilation rate involves several algorithms and physiological variables (U.S. EPA, 2012a,b). As described in section 3.4.3, we are nearing completion of an updated approach to estimate activity-specific $\dot{V}_E$.

4.1.7 Exposure Assessment Estimates

There are several useful indicators of individuals' exposures to various levels of air pollution. Factors that can be important in defining such indicators include the magnitude and duration of exposures, frequency of repeated high exposures, and ventilation rate of the individual at the time of exposure. In this assessment, exposure indicators will include the occurrence of daily maximum 5-minute SO_2 exposures at or above benchmark levels, also stratified by a specified target ventilation rate(s). Given the nature of these indicators with regard to informing potential health risk, details as to the selection of these particular target levels are provided in section 4.2.2.

APEX can calculate two general types of summary exposure estimates: counts of people and person-occurrences. The former counts the number of individuals exposed one or more times per year, several times a year (e.g., 5 or more times) to the exposure indicator (e.g., exposure level and ventilation rate) of interest. In the case where the exposure indicator is a benchmark, the model estimates the number of people who experience that level of air pollution, or higher, at least once during the modeled period. The person-occurrences metric counts the number of times that an individual is exposed to the exposure indicator of interest and then accumulates counts over all individuals. For example, a value of 10 for the person-occurrences measure could be the result of 1 occurrence for 10 people or 10 occurrences for 1 person. Because this latter metric is less informative regarding individual exposures, we do not anticipate reporting this output for this REA.

In summary, APEX modeling outputs for use in this review will include (1) counts of people exposed at least once to a range of short-term peak SO_2 concentrations while at or above a particular exertion level, and (2) counts of people experiencing multiple exposures at or above a particular level while at or above a given exertion level.

4.2 HEALTH RISK CHARACTERIZATION

In this section, we describe the two approaches we will use to characterize potential risk. As in the last review, these approaches are based on the body of evidence from the controlled human exposure studies reporting lung function decrements (as measured by changes in sRaw and FEV_1), as well as changes in other measures of lung function, respiratory symptoms, and various markers of inflammation, in adult study subjects having asthma. For both approaches, staff plans to develop health risk estimates for two groups of individuals with asthma living in the selected study areas: adults with asthma (ages > 18), and school-aged children with asthma (ages 5-18).

4.2.1 Health Endpoints

As in the last review, the evidence of health effects associated with exposure to short-term (5-10 minutes) peak SO_2 exposures is based on findings from controlled human exposure studies of exercising adult individuals with asthma, most of which were conducted in the 1980s and evaluated in the ISA from previous and current NAAQS reviews (2008 ISA; second draft ISA). Specifically, the health endpoints identified in those studies include changes in respiratory function indicative of bronchoconstriction as measured by increased specific airway resistance (sRaw) and decreased forced expiratory volume in one second (FEV_1) observed in subjects with asthma. As summarized in section 2.1.3 above, exercising individuals with asthma exposed to SO_2 concentrations of 200-300 ppb for 5-10 minutes experienced moderate or greater lung function decrements (increases in sRaw ≥ 100%) in 5-30% of tested individuals. Exercising individuals with asthma exposed to SO_2 concentrations of 400-600 ppb for to 5-10 minutes resulted in moderate or greater decrements in lung function in 20-60% of tested individuals. At concentrations ≥ 400 ppb, moderate or greater decrements were frequently accompanied by respiratory symptoms.

This evidence of responses associated with bronchoconstriction in exercising individuals with asthma is the focus of the two approaches to be used to characterize health risk: (1) comparison of exposures at elevated ventilation to exposure concentrations of potential concern (benchmark levels), and (2) lung function risk estimates.

4.2.2 Target Ventilation Rates

As in the last review, we recognize that the target ventilation rate for study subjects (i.e., male and female adults) experiencing effects from 5-10 minute SO_2 exposures in most of the

controlled human exposure studies was approximately between 40-50 L/min (Table 4-6).[53] In order to use this information to estimate health risks for children, the ventilation targets for adults need to be adjusted to best reflect the different physiology of children. One approach to accomplish this is to generate an equivalent ventilation rate (EVR) based on normalizing the simulated individuals' activity-specific ventilation rate to their BSA. Staff has used an EVR in REAs for previous SO_2 and O_3 NAAQS REAs to also identify comparable activity-specific ventilation rates for children and adults (U.S. EPA, 2014b; Whitfield et al., 1996).

As was done in previous REAs, we propose the same approach to be used here. The target ventilation rates from the controlled human exposure study are generally within 40-50 L/min, with most at or around 40 L/min. However, body surface area was not measured in the controlled human exposure studies and the relevant ventilation data were not separated by sex.

Staff assumed a median estimate of BSA of 1.95 m^2 based on data for males and females within the ages of 21-50 from U.S. EPA (2011) were reasonable estimates of the study subjects. Based on these data, an EVR = 40/1.95 ≈ 21 L/min-m^2 will be used to characterize an equivalent target ventilation rate in this assessment. Thus, individuals at or above an EVR of 21 L/min-m^2 (children or adult) for a 5-minute exposure event are characterized as performing activities at or above moderate exertion. This EVR is slightly lower than that used in the 2009 SO_2 REA (i.e., 22 /min-m^2) because the BSA (1.8 m^2) approximated at that time was based on data from U.S. EPA (1997), thus possibly comprised of a relatively fitter population.

4.2.3 Exposure Benchmark-Based Health Risk

As in the last review (as described in section 2.4.3 above), one of the risk metrics to be estimated will be based on comparisons of estimates of 5-minute exposures experienced while at an elevated ventilation rate to benchmark levels based on the controlled human exposure studies. In addition to its use in the 2009 SO_2 REA, this approach has been used in past O_3 REAs (e.g., U.S. EPA, 2014b). In the subsections that follow, each of these elements are evaluated and defined to objectively inform the characterization of the potential health risk associated with the APEX simulated individuals' exposure events.

4.2.3.1 Benchmark Levels

As in the 2009 REA, we have identified a set of benchmarks to represent "exposures of potential concern" (75 FR 35527, June 22, 2010), 5-minute concentrations for which there is potential for a respiratory response indicative of some level of bronchoconstriction to occur in an

[53] Note that study subjects were free-breathing; thus it is expected that there was a mixture of nasal, oral, and oro-nasal breathing that occurred across the study subjects. Without information regarding the precise breathing method used by any subject corresponding with their health response, staff assumed that the mixture in breathing method used by study subjects is representative for the simulated population.

exposed individual, with the potential and the severity varying with the magnitude of the benchmark level. These levels are derived solely from the controlled human exposure studies, which can examine the health effects of SO_2 in the absence of co-pollutants that typically can confound results in epidemiologic analyses; thus, health effects observed in such controlled studies can confidently be attributed to a defined exposure level of SO_2.

Considering this information, as described in the second draft ISA and summarized in section 2.2.3 above, staff concludes that it is appropriate, as in the last review, to use four benchmark levels: 100, 200, 300 and 400 ppb. As recognized in the last review, we consider exposures with respect to the 200 and 400 ppb 5-minute benchmark levels to be of particular interest because: (1) 400 ppb represents the lowest concentration in free-breathing controlled human exposure studies where moderate or greater lung function decrements occurred which were often statistically significant at the group mean level and were frequently accompanied by respiratory symptoms; and (2) 200 ppb is the lowest level at which moderate or greater lung function decrements in free-breathing controlled human exposure studies were found in some individuals, although these lung function changes were not statistically significant when evaluated considering the group mean level (75 FR 35527, June 22, 2010). The lowest level (100 ppb) has been identified in consideration of the data showing moderate or greater lung function decrements at the lowest exposure concentration tested in free breathing exposure studies (200 ppb) and of the very limited data indicating some potential for SO_2-induced lung function decrements in individuals with asthma[54] exposed to 100 ppb SO_2 administered via mouthpiece[55] (second draft ISA, section 5.2.1).

4.2.3.2 Exposure Benchmark-based Risk Results

APEX estimates of personal exposure will be compared to the health benchmark levels, considering also that the exposures occurred while at or above the target ventilation rate, an approach best resembling the conditions of the controlled human exposure study. As described in

[54] We have also considered the evidence with regard to the response of individuals with severe asthma that are not generally represented in the full set of controlled human exposure studies. There is no evidence to indicate such individuals would experience moderate or greater lung function decrements at lower SO_2 exposure concentrations than individuals with moderate asthma. With regard to the severity of the response, the limited data that are available indicate a similar magnitude SO_2-specific response (in sRAW) as that for individuals with less severe asthma, although the individuals with more severe asthma are indicated to have a greater response to exercise prior to SO_2 exposure, indicating that those individuals "may have more limited reserve to deal with an insult compared with individuals with mild asthma" (second draft ISA, p. 5-21).

[55] Studies utilizing a mouthpiece to deliver pollutant concentrations cannot be directly compared to studies involving freely breathing subjects, as nasal absorption of SO_2 is bypassed during oral breathing, thus allowing a greater fraction of inhaled SO_2 to reach the tracheobronchial airways. As a result, individuals exposed to SO_2 through a mouthpiece are likely to experience greater respiratory effects from a comparable SO_2 exposure using free breathing.

section 4.2.1, when the exposure outcome is linked with the appropriate exertion level, a more appropriate indicator of potential health risk is generated than when compared with an approach that considers ambient air concentrations or exposures alone. Thus, the time-series of exposures for each APEX-simulated individual will be used to identify the daily maximum 5-minute SO_2 concentrations that occur while at moderate or greater exertion. We will focus on the daily maximum 5-minute exposure relative to the benchmark levels to capture the maximum potential response an individual would experience in a given day, rather than comparing all 5-minute exposures to each benchmark. While there is limited evidence that the SO_2-specific bronchoconstriction response is transient, such that similar responses might be expected from two appropriately-separated exposures in the same day (e.g., Linn et al., 1984; Linn et al., 1987), the interpretation of the multiple occurrences within a day could be complicated by the need to consider other factors, such as duration of both the exposure and associated elevated activity level, as well as disease status (second draft ISA, section 5.2.1). Based on all of the instances when a daily maximum 5-minute exposure (while at or above the target EVR) is above a benchmark level, APEX will then summarize the individual-level information and generate a population-based, study area statistic indicating the number (and percent) of simulated persons experiencing exposures at or above the particular benchmark levels of interest, while at moderate or greater exertion.[56]

4.2.4 Lung Function Decrement-based Health Risk

The lung function risk assessment will involve an estimation of the number of people expected to experience a specific lung function effect and the total number of occurrences of these effects per individual across the simulation period. Thus two risk metrics are generated. The first would indicate the number and percent of people estimated to at least one lung function decrement in a year. The second risk metric would indicate the number and percent of people experiencing multiple lung function decrements associated with SO_2 concentrations. This assessment requires the combining of E-R functions discussed below (section 4.2.4.1) with the exposures estimates for the relevant exposure duration (5 minutes) and exertion level.

4.2.4.1 Development of Exposure-Response Functions

The health risk assessment conducted in this new review will build on the approach developed and applied in the 2009 REA. In that assessment, risk estimates were developed for

[56] A 'person-days' risk metric can also be generated by APEX, indicating the total number of exceedances across the modeling domain and time period assessed as a whole, but this metric is less informative for the purposes of the review. The metric conflates the variability in individual exposures (this can be wide ranging depending on the occurrence of peak concentrations and the distribution of time spent outdoors for modeled individuals), and from a physiological perspective, creates an uninterpretable aggregate population exposure metric.

lung function responses associated with 5-minute exposures while engaged in moderate or higher exertion. These estimates were based on E-R relationships estimated from the combined data sets from multiple controlled human exposure studies. The data from these studies were corrected for effects observed with exposure to clean air to remove any systematic bias that might be present in the data attributable to exercise, diurnal variation, or other effects, in addition to those attributed by exposure to SO_2, during the course of an exposure.

The E-R functions will be derived by applying a regression approach to these data for the selected health endpoints. Probit and logistic regression techniques have been used previously to mathematically describe the E-R relationship (2009 SO_2 REA, section 9.2.3). We plan to use the probit model for this risk analysis based on comments from CASAC on the use of this approach in the 2009 REA (Samet, 2009, p. 14).[57] Because there are fewer clinical data for FEV_1 than for sRaw (second draft ISA, Table 5-2) and there is greater physiological specificity in the sRaw measurement compared to that of the FEV_1, we will estimate health risk only using the sRaw data in this assessment. This reasoning and conclusion is consistent with that of the last review. Whereas FEV_1 risk estimates were calculated and presented in the 2009 REA, they were given less weight than risk estimates based on sRaw in considerations for the review (2009 REA, chapter 10; 75 FR 35520).

To evaluate health risk in this assessment, we will estimate numbers and percent of study groups expected to experience moderate or greater lung function decrements, in terms of increases in sRaw at or above 100% and at or above 200%, as a result of exposures to SO_2 from ambient air. There are two controlled human exposure studies of the effects of SO_2 on lung function that were not used in the 2009 REA analyses (Linn et al., 1983; Horstman et al., 1986).[58] These studies, in addition to the studies used in the 2009 REA, will be included in the dataset used to derive the E-R functions. Table 4-6 presents study summary data for changes in sRaw from all references from which individual data are available, for free-breathing studies. To illustrate the E-R relationship indicated by these data, the percent of the study populations experiencing changes in sRaw (ΔsRaw) $\geq$ 100% is plotted in Figure 4-7, where the points are annotated with the number of subjects from each study.

The data used, of course, are important in determining the E-R function. Of particular interest is how the function extends below exposures for which we have controlled human

[57] From Samet, 2009 (p. 14): "Another issue for clarification is the choice to base predictions of sRaw responses only on a fit to the logistic model. A probit model fit is considered but the discussion is based only on goodness-of-fit criteria which are reportedly equivalent between the two models. This neglects the *a priori* reason to prefer the probit model (based on a hypothesized lognormal distribution of individual thresholds for response)."

[58] The individual-level data from Linn et al (1983) were not available at the time of the 2008 ISA. The Horstman et al. 1986 data were interpreted based on the figures provided in that paper indicating individual responses.

exposure data (i.e., < 200 ppb). In the 2009 REA, apportioning of the risk by the selected exposure levels indicated that low level 5-minute exposures (e.g., 0-50 ppb, 50-100 ppb, 100-150 ppb, etc.) can contribute to a large portion (50% or more) of the estimated risk depending on the air quality scenario (e.g., 2009 REA, Figure 9-8). For instance, the range of SO_2 exposures and associated responses included from the higher end can have varying influence on the E-R function at the lower end. To demonstrate this, we derived the function using two data sets: one E-R function derived using all of the data in Table 4-6 and one derived without using the 1000 ppb exposure results. For each respective function, the associated model predictions were generated at 5 ppb exposure increments, indicating the response probabilities at each exposure level. Table 4-7 provides the results of this comparison for exposures at or below 100 ppb. Based on these preliminary analyses, it can be seen that the choice of data used to derive the E-R function can influence the percent of the population estimated to have a response by a factor of 2 or more. How this can influence the number of simulated individuals is not known at this time, however, we expect to perform additional analyses of the E-R function such as this, along with others, to provide additional perspective in the current REA.

Table 4-6. Summary of controlled human exposure studies containing individual response data: number and percent of individuals who experienced greater than or equal to a 100 or 200 percent increase in specific airway resistance (sRaw), adjusted for effects of exercise in clean air.

SO_2 (ppb)	Exposure duration (minutes)	N	Ventil-ation (l/min)	sRaw ≥100 (N)	sRaw ≥200 (N)	sRaw ≥100 (%)	sRaw ≥200 (%)	Reference
200	5	23	~48	2	0	8.7%	0.0%	Linn et al. (1983)[a]
200	10	40	~40	3	1	7.5%	2.5%	Linn et al. (1987)[b]
250	5	19	~50-60	6	3	31.6%	15.8%	Bethel et al. (1985)
250	5	9	~80-90	2	0	22.2%	0.0%	Bethel et al. (1985)
250	10	27	~42	0	0	0.0%	0.0%	Horstman et al. (1986)[a]
250	10	28	~40	1	0	3.6%	0.0%	Roger et al. (1985)
300	10	20	~50	2	1	10.0%	5.0%	Linn et al. (1988)
300	10	21	~50	7	2	33.3%	9.5%	Linn et al. (1990)
400	5	23	~48	3	1	13.0%	4.3%	Linn et al. (1983)[a]
400	10	40	~40	9.5	3.5	23.8%	8.8%	Linn et al. (1987)[b]
500	5	10	~50-60	6	4	60.0%	40.0%	Bethel et al. (1983)
500	10	27	~42	6	1	22.2%	7.4%	Horstman et al. (1986)[a]
500	10	28	~40	5	1	17.9%	3.6%	Roger et al. (1985)
600	5	23	~48	9	6	39.1%	26.1%	Linn et al. (1983)[a]
600	10	40	~40	13.5	9.5	33.8%	23.8%	Linn et al. (1987)[b]
600	10	20	~50	12	7	60.0%	35.0%	Linn et al. (1988)
600	10	21	~50	13	6	61.9%	28.6%	Linn et al. (1990)
1000	10	10	~40	6	2	60.0%	20.0%	Kehrl et al. (1987)
1000	10	28	~40	14	7	50.0%	25.0%	Roger et al. (1985)
1000	10	27	~42	15	7	55.6%	25.9%	Horstman et al. (1986)[a]

From second draft ISA Table 5-2, Figure 5-1.

Data presented from all references from which individual data were available. Percentage of individuals who experienced greater than or equal to a 100 or 200% increase in specific airway resistance (sRaw). Lung function decrements are adjusted for the effects of exercise in clean air (calculated as the difference between the percent change relative to baseline with exercise|SO_2 and the percent change relative to baseline with exercise|clean air).

[a] Data were not used to develop the E-R function in the 2009 SO2 REA.

[b] Responses of mild and moderate asthmatics reported in Linn et al. (1987) are the average of the first and second round exposure responses following the first 10 min period of exercise.

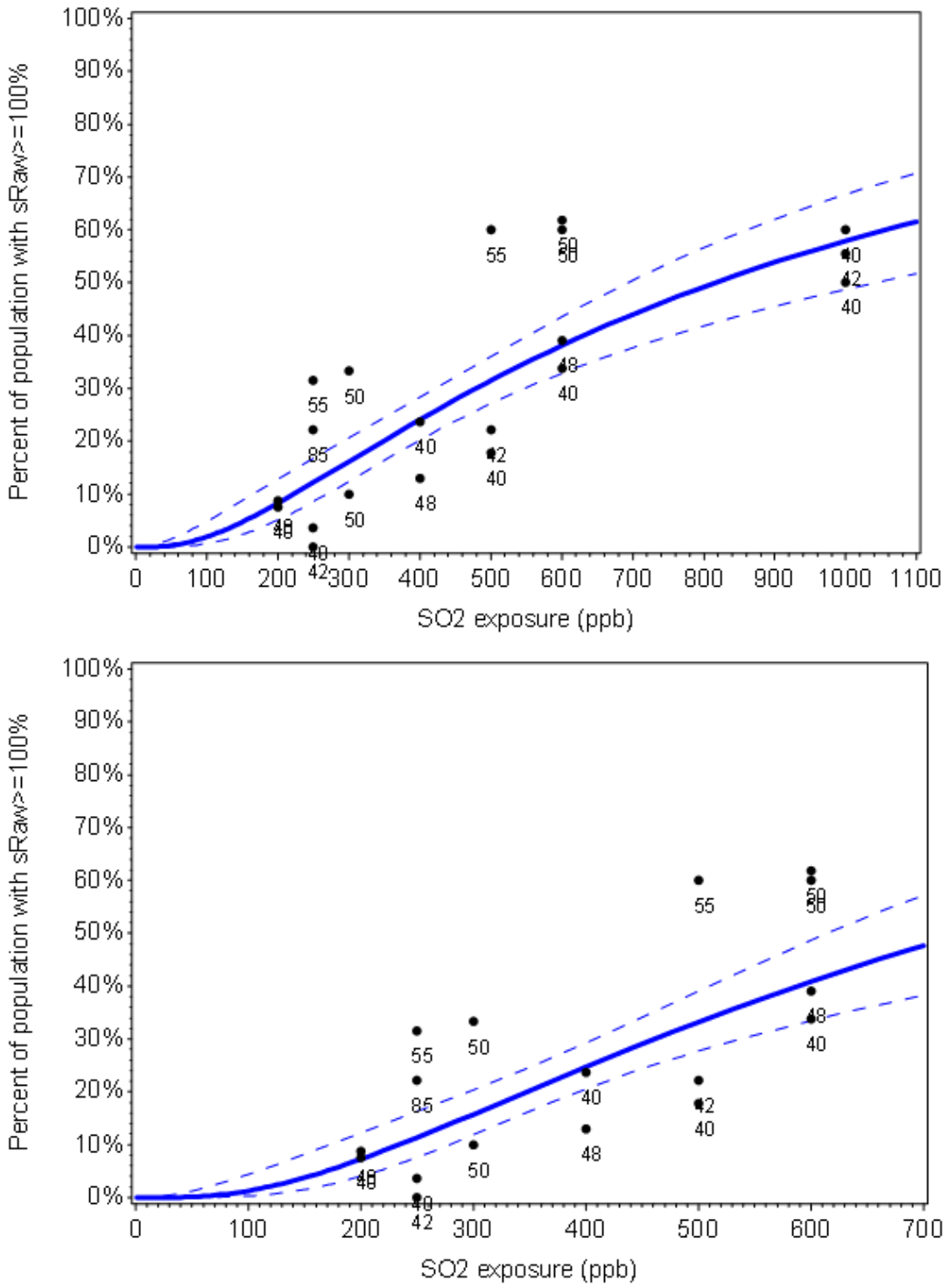

Figure 4-7. Percent of individuals experiencing changes in sRaw ≥ 100% using controlled human exposure study data (Table 4-6) fit using a probit regression (solid line). Annotated with the number of study subjects from each study, dashed line indicates a 5th and 95th percentile prediction interval for the mean. Models for SO_2 exposures from 200-1,000 ppb (top panel) and for SO_2 exposures from 200-600 ppb (bottom panel).

Table 4-7. Estimated percent of the population experiencing sRaw ≥ 100% considered at 5 ppb increments and using two different data sets to derive the E-R function: one using all SO_2 exposures, the other using only SO_2 exposures between 200-600 ppb.

SO_2 Exposure	Percent of the **Population with sRaw ≥ 100%**	
	ER function prediction using 200-1,000 ppb SO_2 exposures	ER function prediction using 200-600 ppb SO_2 exposures
0	1.9E-11	8.2E-14
5	2.5E-07	1.2E-08
10	7.0E-06	7.8E-07
15	4.0E-05	6.8E-06
20	1.3E-04	2.8E-05
25	2.9E-04	7.8E-05
30	5.6E-04	1.7E-04
35	9.5E-04	3.3E-04
40	1.5E-03	5.7E-04
45	2.1E-03	8.9E-04
50	2.9E-03	1.3E-03
55	3.9E-03	1.9E-03
60	5.0E-03	2.5E-03
65	6.3E-03	3.3E-03
70	7.7E-03	4.3E-03
75	9.3E-03	5.3E-03
80	1.1E-02	6.5E-03
85	1.3E-02	7.9E-03
90	1.5E-02	9.4E-03
95	1.7E-02	1.1E-02
100	1.9E-02	1.3E-02

4.2.4.2 Lung Function Decrement-based Health Risk Results

Staff plans to generate two risk metrics for each of the lung function response definitions, ΔsRaw ≥ 100% and ΔsRaw ≥ 200%, as was done in the 2009 REA. The first risk metric will be the number of individuals (e.g., children with asthma) estimated to experience at least one lung function response in the designated population in a year associated with SO_2 concentrations under a given air quality scenario. The second risk metric will be the number of individuals experiencing multiple lung function responses in a year. To calculate this measure of risk we use the number of exposures (concomitant with moderate or greater exertion) among the population that are at or above each of a set of exposure concentrations estimated from the exposure modeling. As described previously, in this assessment we are using finer-scale exposure

designations, particularly at exposures below 200 ppb, to better capture the variation that may correspond to both the changes in the percent of individuals responding as well as the expected variation occurring in number of individuals exposed from one exposure bin to another. For exposures <150 ppb, the exposure bins will be set at 10 ppb increments (e.g., 10–20 ppb, 20–30 ppb, etc.), exposures ≥150 and <200 ppb will be at 20 ppb increments, exposures ≥200 and <300 ppb will be at 25 ppb increments, and exposures ≥300 ppb using 50 ppb increments. From this we calculate the number of exposures within each exposure bin. We then calculate the number of occurrences of lung function response by multiplying the number of exposures in an exposure bin by the response probability (given by the probit E-R function for the specified definition of lung function response) associated with the midpoint of that bin (e.g., the midpoint of the 10-20 ppb bin is 15 ppb, thus the frequency/probability obtained from the probit function at 15 ppb will be used to estimate the number of persons responding). Results for all bins will be summed to generate the total estimated risk. Additionally, because we will have the risk estimates effectively apportioned to the exposure bins, the contribution to risk estimates from each exposure bin will also be provided.

4.3 ASSESSMENT OF VARIABILITY AND CHARACTERIZATION OF UNCERTAINTY

An important issue associated with any population exposure and risk assessment is the assessment of variability and characterization of uncertainty. Variability refers to the inherent heterogeneity in a population or variable of interest (e.g., residential air exchange rates). The degree of variability cannot be reduced through further research, only better characterized with additional measurement. Uncertainty refers to the lack of knowledge regarding the values of model input variables (i.e., parameter uncertainty), the physical systems or relationships used (i.e., use of input variables to estimate exposure or risk or model uncertainty), and in specifying the scenario that is consistent with purpose of the assessment (i.e., scenario uncertainty). Uncertainty is, ideally, reduced to the maximum extent possible through improved measurement of key parameters and iterative model refinement. The following two sections describe the approaches we will use to assess variability and to characterize uncertainty in this REA. The primary outcome will be a summary of variability and uncertainty evaluations conducted to date regarding our SO_2 exposure assessments and APEX exposure modeling and to identify the most important elements of uncertainty in need of further characterization. Each section will contain a concise tabular summary of the identified components and how, for elements of uncertainty, each source may affect the estimated exposures.

4.3.1 Assessment of Variability and Co-variability

The goal in addressing variability in the REA will be to ensure that the estimates of exposure and risk reflect the variability of SO_2 concentrations in ambient air, population characteristics, associated SO_2 exposures, physiological characteristics of simulated individuals, and potential health risk across the study areas and for the simulated at-risk populations. In the REA, there are several algorithms that we plan to use to account for variability of input data when generating the number of estimated benchmark exceedances or health risk outputs. For example, variability may arise from differences in the population residing within census tracts (e.g., age distribution) and the activities that may affect population exposure to SO_2 (e.g., time spent outdoors, performing moderate or greater exertion level activities outdoors). A complete range of potential exposure levels and associated risk estimates can be generated when appropriately addressing variability in exposure and risk assessments; note however that the range of values obtained would be within the constraints of the input parameters, algorithms, or modeling system used, not necessarily the complete range of the true exposure or risk values.

We note also that correlations and non-linear relationships between variables input to the model can result in the model producing inaccurate results if the inherent relationships between these variables are not preserved. That is why APEX is also designed to account for co-variability, or linear and nonlinear correlation among the model inputs, provided that enough is known about these relationships to specify them. This is accomplished by providing inputs that enable the correlation to be modeled explicitly within APEX. For example, there is a non-linear relationship between the outdoor temperature and air exchange rate in homes. One factor that contributes to this non-linear relationship is that windows tend to be closed more often when temperatures are at either low or high extremes than when temperatures are moderate. This relationship is explicitly modeled in APEX by specifying different probability distributions of air exchange rates for different ambient air temperatures.

In any event, important sources of the variability and co-variability accounted for by APEX and used for this SO_2 exposure analysis will be identified and summarized. Where possible, staff will identify and incorporate the observed variability in input data sets rather than employing standard default assumptions and/or using point estimates to describe model inputs. Where appropriate for this REA, we will begin with descriptions regarding variability distributions used for the last O_3 REA and also acknowledge particular variabilities associated with some of the algorithms and processes in the version of APEX which we apply.

4.3.2 Characterization of Uncertainty

While it may be possible to capture a range of exposure or risk values by accounting for variability inherent to influential factors, the true exposure or risk for any given individual within

a study area may be unknown, though can be estimated. To characterize health risks, exposure and risk assessors commonly use an iterative process of gathering data, developing models, and estimating exposures and risks, given the goals of the assessment, scale of the assessment performed, and limitations of the input data available. However, significant uncertainty often remains and emphasis is then placed on characterizing the nature of that uncertainty and its impact on exposure and risk estimates.

Above we summarized the most important uncertainties potentially affecting the exposure estimates reported in the 2009 REA and how we can address some of them using newly available information. Additionally, the REAs conducted for the most recent NO_2 (U.S. EPA, 2008), carbon monoxide (U.S. EPA, 2010), and O_3 (U.S. EPA, 2014b) also characterized the uncertainties associated with APEX exposure modeling (among other pollutant specific issues). Conclusions drawn from each of these characterizations, and considering these in light of new information and approaches used for the REA, and any new evaluations performed in the current REA will be synthesized following the approach outlined by WHO (2008) and used to identify, evaluate, and prioritize the most important uncertainties relevant to the estimated exposure and risk outcomes. Staff plan to use a mainly qualitative approach supplemented by various model sensitivity analyses and input data evaluations, all complementary to quantitative uncertainty characterizations conducted for the 2007 O_3 REA by Langstaff (2007).

The approach to be used here varies from that described by WHO (2008) in that a greater focus will be placed on evaluating the direction and the magnitude[59] of the uncertainty; that is, qualitatively rating how the source of uncertainty, in the presence of alternative information, may affect the estimated exposures and health risk results. Following the identification of key uncertainties, staff will subjectively scale the overall impact of the uncertainty by considering the relationship between the source of uncertainty and the exposure concentrations (e.g., low, moderate, or high potential impact). Also to the extent possible, staff will also include an assessment of the direction of influence, indicating how the source of uncertainty could affect estimated exposures or risk estimates (e.g., the uncertainty could lead to over- or under-estimates). Further, and consistent with the WHO (2008) guidance, staff will discuss the uncertainty in the knowledge base (e.g., the accuracy of the data used, acknowledgement of data gaps) and decisions made where possible (e.g., selection of particular model forms). The output of the uncertainty characterization will be a summary describing, for each identified source of uncertainty, the magnitude of the impact and the direction of influence the uncertainty may have on the exposure and risk characterization results.

[59] This is synonymous with the "level of uncertainty" discussed in WHO (2008), section 5.1.2.2.

The following summarizes two potential sensitivity analyses concerning input data, output data, or model aspects that may, as feasible, be conducted in addition to the base level analyses described above.

- Because there is uncertainty in the risk estimated for exposures below 200 ppb and we will have risk estimates associated with numerous exposure bins, we will present complementary risk estimates that assume the particular contribution from an exposure bin is negligible (e.g., assume a threshold at 10 ppb, such that for all people having their daily maximum 5-minute exposure < 10 ppb, none will be estimated as having an sRaw response of interest).
- For the benchmark analysis and for identifying exposure bins used in the risk estimation, exposures of interest are those that occur while at moderate or greater exertion (i.e., have an EVR = 21 L/min-m^2). There are a number of uncertainties associated with the development of this threshold, including the estimation of body surface area and the target ventilation rate. We plan to explore these and any other influential factors that might influence this selected value, based on any relevant and available information in the controlled exposure studies and other published studies.

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APPENDIX A. CONSIDERATION OF SUPPORT IN NEWLY AVAILABLE INFORMATION FOR QUANTITATIVE ASSESSMENT OF OTHER ASTHMA-RELATED HEALTH OUTCOMES

Additional endpoints for asthma-related* health effects		
Endpoints	Information Newly Available in this Review	Consideration of Potential Utility and Impact on Quantitative Exposure/Risk Assessment
A. The following endpoints have "[g]enerally supporting evidence from multiple epidemiologic studies at relevant SO_2 concentrations" (second draft ISA, Table 5-51).		
1. Emergency department visits and Hospitalizations	1. There are four new U.S. studies identified in the second draft ISA for asthma-related emergency department visits (Strickland et al., 2010; Byers et al., 2015; Alhanti et al., 2015; Li et al., 2011; second draft ISA Section 5.2.1). One of these studies is a multi-city study. Three of the four studies use 1-hour maximum concentrations as the exposure metric. In the previous review, this metric was only used in the Peel et al. (2005) study. All four of these studies have effects estimates for children (< 18 years of age), and one contains effect estimates for adults aged 65 and above, though those results show a negative association (Alhanti et al., 2015). In the previous review, there were only single-city U.S. studies. In the current review, there is one study that reports effect estimates for three U.S. cities (Alhanti et al., 2015). New studies provide some evidence of seasonal differences, with higher effect estimates in warmer months (Strickland et al., 2010; Byers et al., 2015). The Strickland et al. (2010) and Li et al. (2011) studies provide evidence for a linear, no-threshold relationship between SO_2 concentrations and emergency department visits among children with asthma. There were no new U.S hospitalization studies among asthmatics identified.	1. Staff concludes that there is little utility for risk estimates based on such studies considering the strength of the epidemiologic evidence and lack of exposure information, particularly in light of the greater confidence in an exposure-based risk assessment. Furthermore, none of these new studies reduce previously identified uncertainties specifically related to potential copollutant confounding, and often the study designs were not specific to SO_2, suggesting that SO_2-exposure considerations, including the localized nature of the pollutant (i.e potential concentration gradients), were often not accounted for. (second draft ISA; 2009 REA, p. 58)
2. Respiratory symptoms among children (e.g., wheeze)	2. Two new U.S. studies were identified in the ISA (Spira-Cohen et al., 2013; O'Connor et al., 2008; second draft ISA, Section 5.2.1)	2. These studies do not report concentrations, making comparisons and interpretation difficult, and limiting utility in a risk assessment, and O'Connor et al. (2008) analyzes 19-day average SO_2 concentrations, which are more subject to residual temporal confounding (second draft ISA, p. 5-45)
B. Additional endpoints include: (1) outpatient and physician visits for upper and lower respiratory infection (2) airway inflammation and oxidative stress, and (C) airway responsiveness. Given the ISA conclusion that these endpoints have "[l]imited and inconsistent evidence across disciplines and outcomes," as well as inconsistencies and/or limitations of the studies available for each endpoint, we do not find this information to provide necessary support for use in quantitative risk assessment (second draft ISA, Table 5-21).		
* With regard to additional evidence on nonasthma-related respiratory effects, the ISA notes that "The limited and inconsistent evidence for these nonasthma-related respiratory effects does not contribute heavily to the causal determination," (second draft ISA, section 5.2.1.9).		

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APPENDIX B. OCCURRENCES OF 5-MINUTE SO_2 CONCENTRATIONS OF INTEREST IN THE RECENT AMBIENT AIR MONITORING DATA (2013-2015)

Preface: The figures included in this appendix illustrate preliminary analyses of air quality data for the years 2013-2015.

The raw data came from pre-generated AQS extract files. Files are located at http://www.epa.gov/airquality/airdata/ad_data.html. Documentation of files is located at http://aqsdr1.epa.gov/aqsweb/aqstmp/airdata/FileFormats.html. Hourly Data Files were used. A separate Hourly Data File for each parameter and year combination was run. The type of SO_2 data is determined by the parameter code and duration code and is coded as follows:

- 1-hour values data - parameter code = 42401 and duration code = 1
- 5-minute data (12 observation per hour) - parameter code = 42401 and duration code = H
- 5-minute data (hourly max) – parameter code = 42406 and duration code = 1

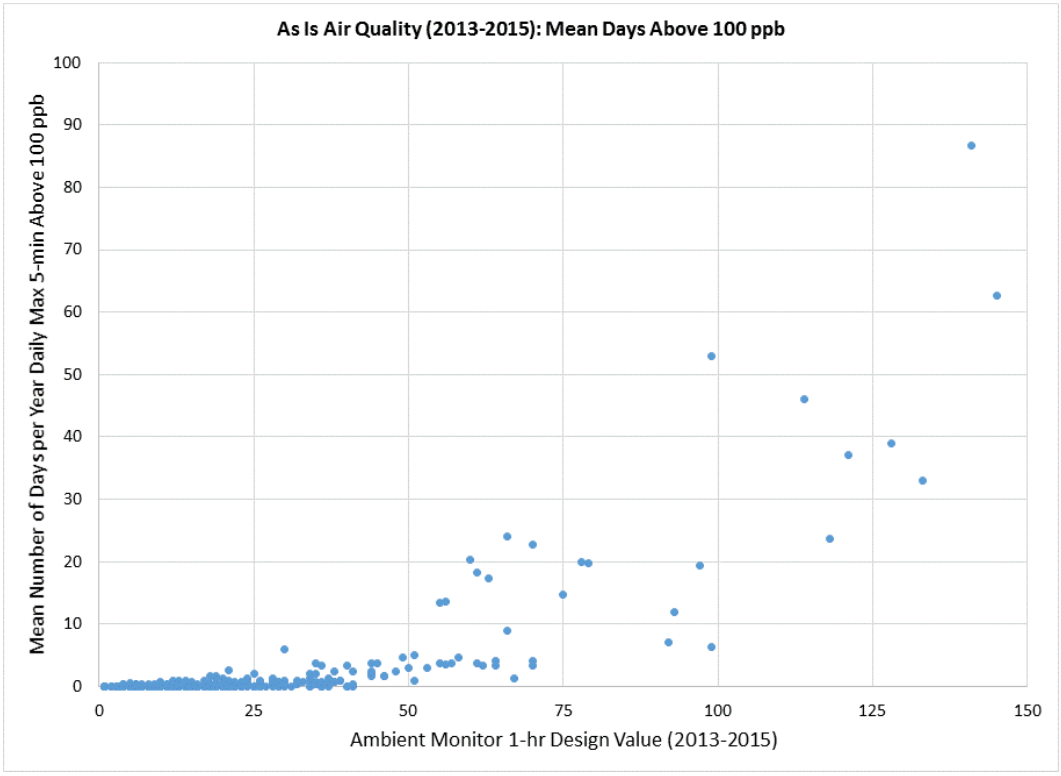
For the 1 hour data at a Site/POC to be used, it must have met the following completeness criteria:

- 75% or more of the hourly observations in a day (18 or more) must be present.
- 75% or more of the days in a quarter must be present and complete:
- 1st Quarter – 68 observations or 69 observations in leap year
  - 2nd Quarter – 69 observations
  - 3rd Quarter – 69 observations
  - 4th Quarter – 69 observations
- 4 quarters for each of at least 3 of the 5 years (2011-2015) must be present and complete. For this analytical purpose, the three years do not have to be consecutive. This dataset was prepared in June 2016.

The following figures display the monitor-year combinations that meet these completeness criteria and for which there are some 5-minute data.

Consideration of these presentations should bear in mind that for this preliminary analysis, completeness criteria were not applied in the interests of displaying all the available information.

Figure B-1. As is (unadjusted) SO_2 monitoring data (2013-2015). Mean number of days/year (top panel) and maximum number of days/year (bottom panel) with daily maximum 5-minute concentrations of SO_2 above 100 ppb.



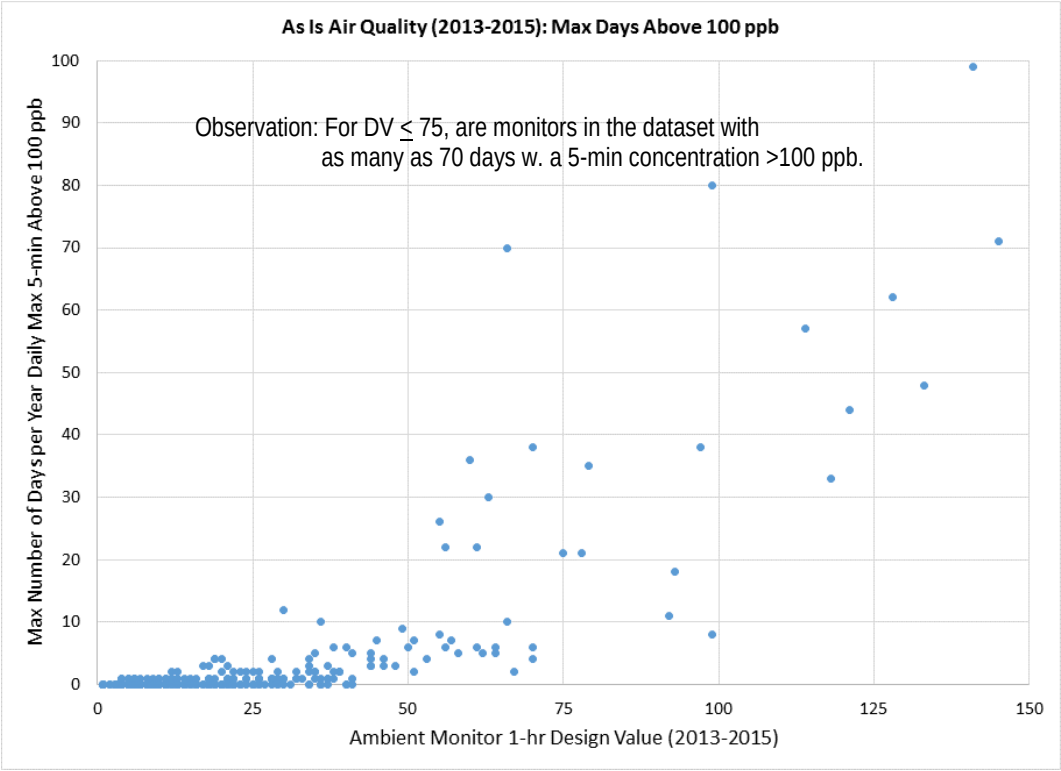
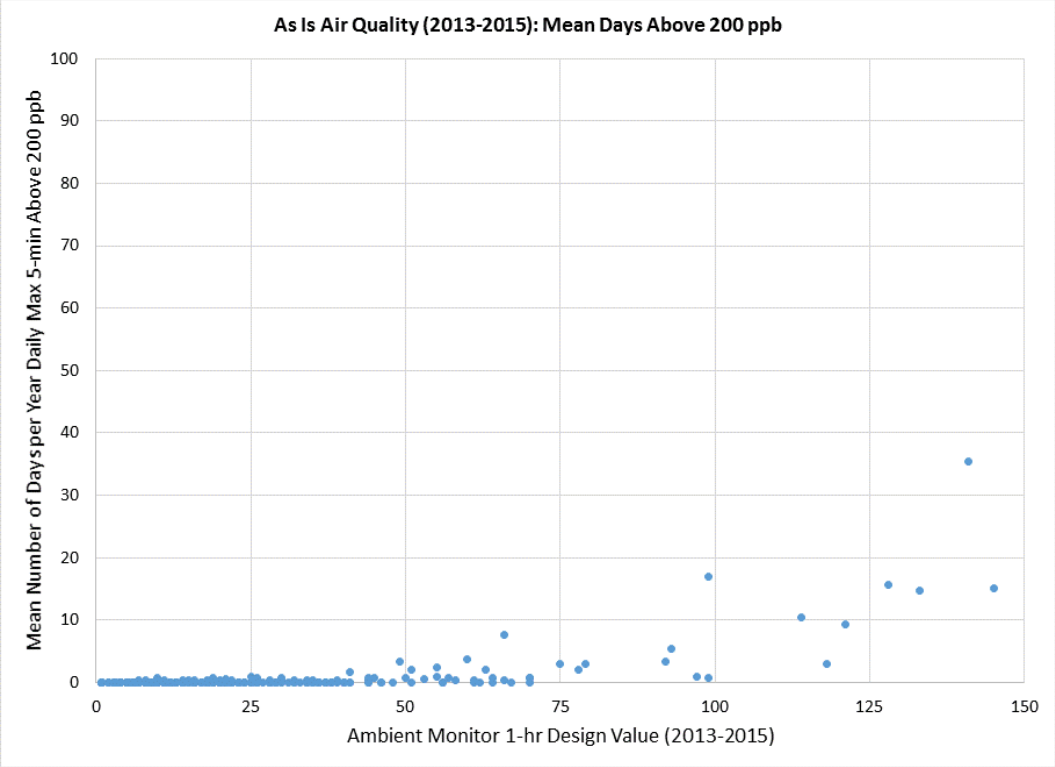


Figure B-2. As is (unadjusted) SO_2 monitoring data (2013-2015). Mean number of days/year (top panel) and maximum number of days/year (bottom panel) with daily maximum 5-minute concentrations of SO_2 above 200 ppb.



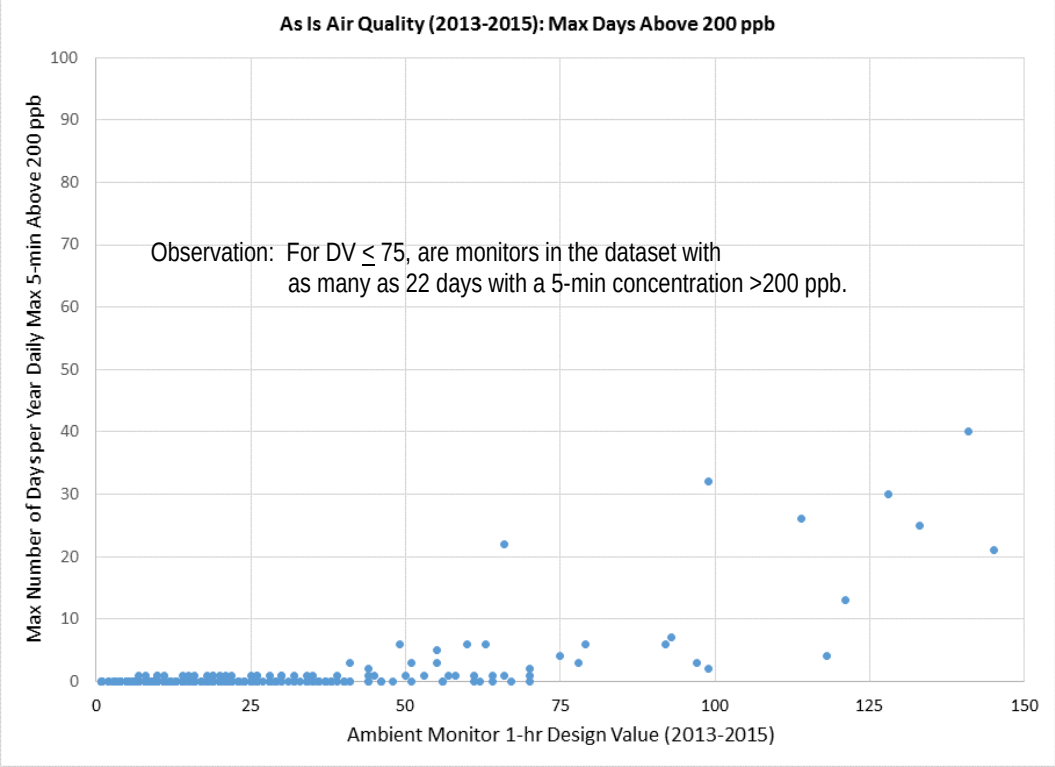
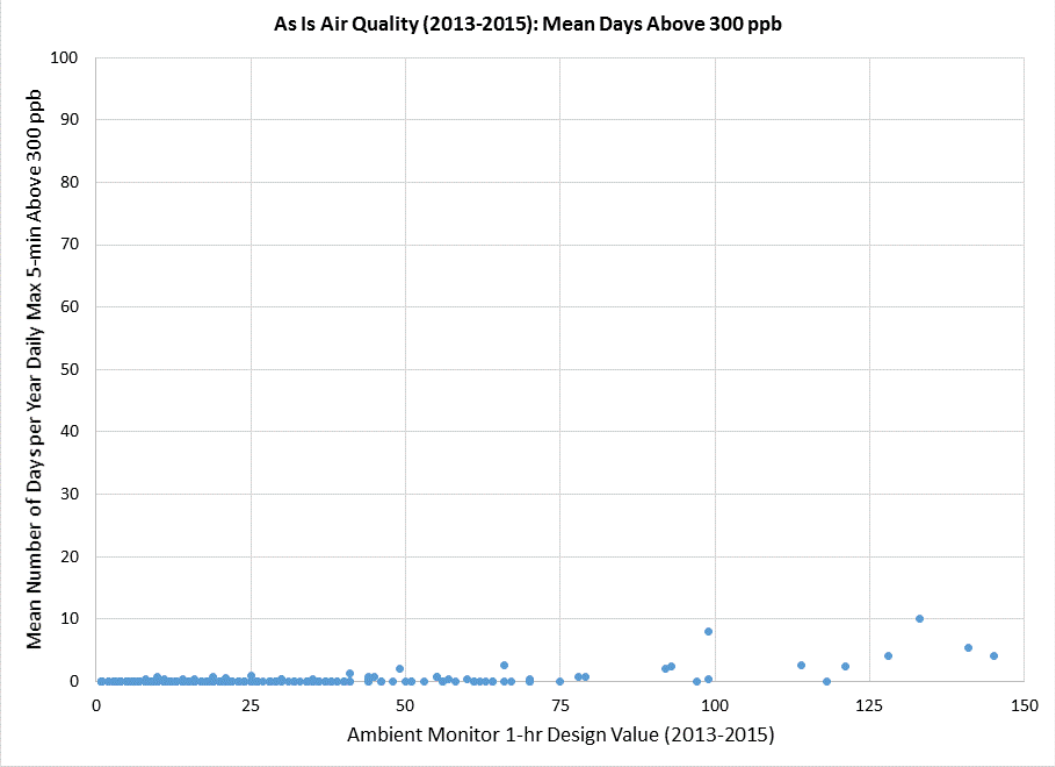


Figure B-3. As is (unadjusted) SO_2 monitoring data (2013-2015). Mean number of days/year (top panel) and maximum number of days/year (bottom panel) with daily maximum 5-minute concentrations of SO_2 above 300 ppb.



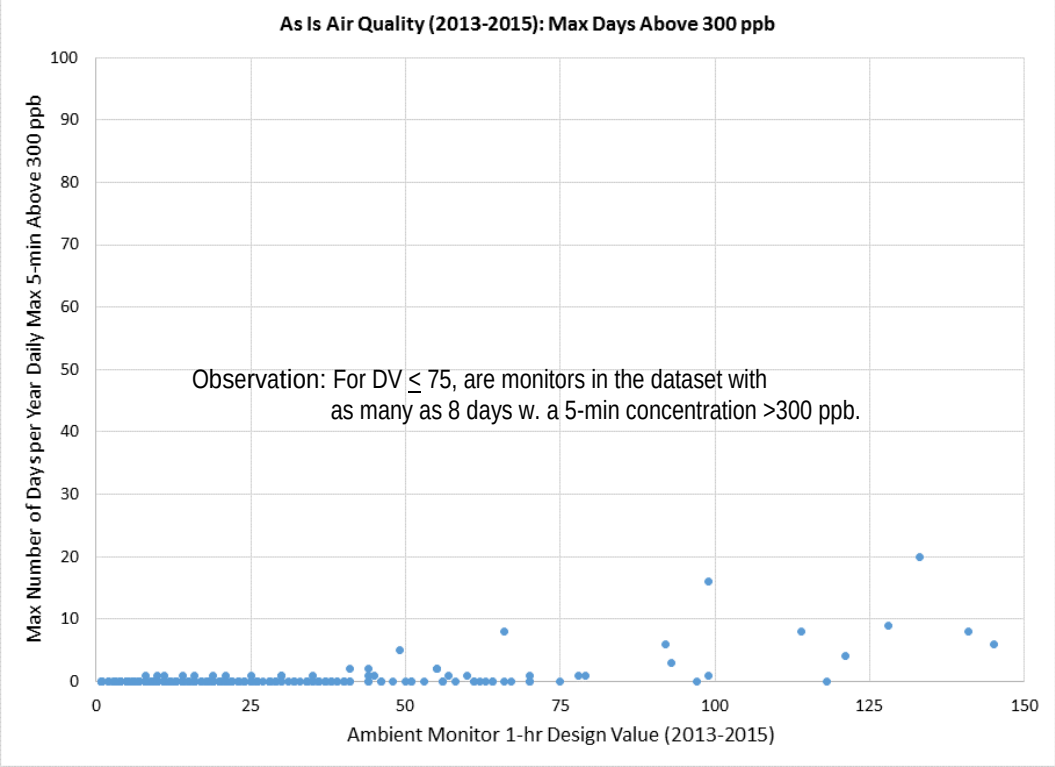
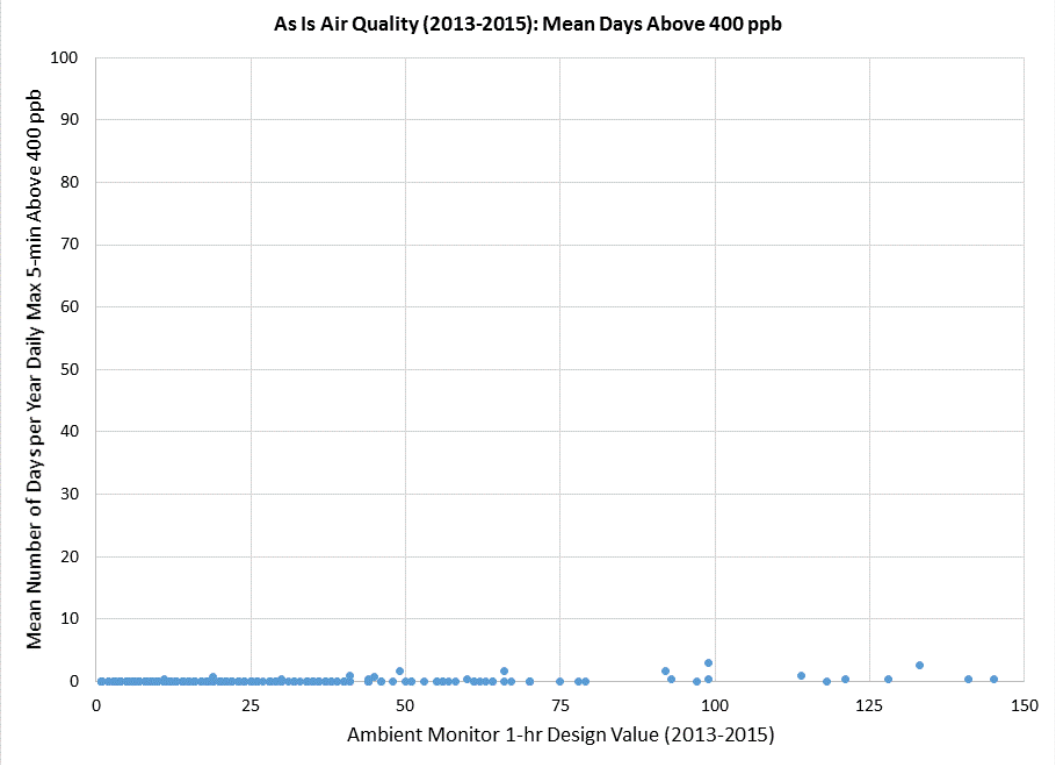


Figure B-4. As is (unadjusted) SO_2 monitoring data (2013-2015). Mean number of days/year (top panel) and maximum number of days/year (bottom panel) with daily maximum 5-minute concentrations of SO_2 above 400 ppb.



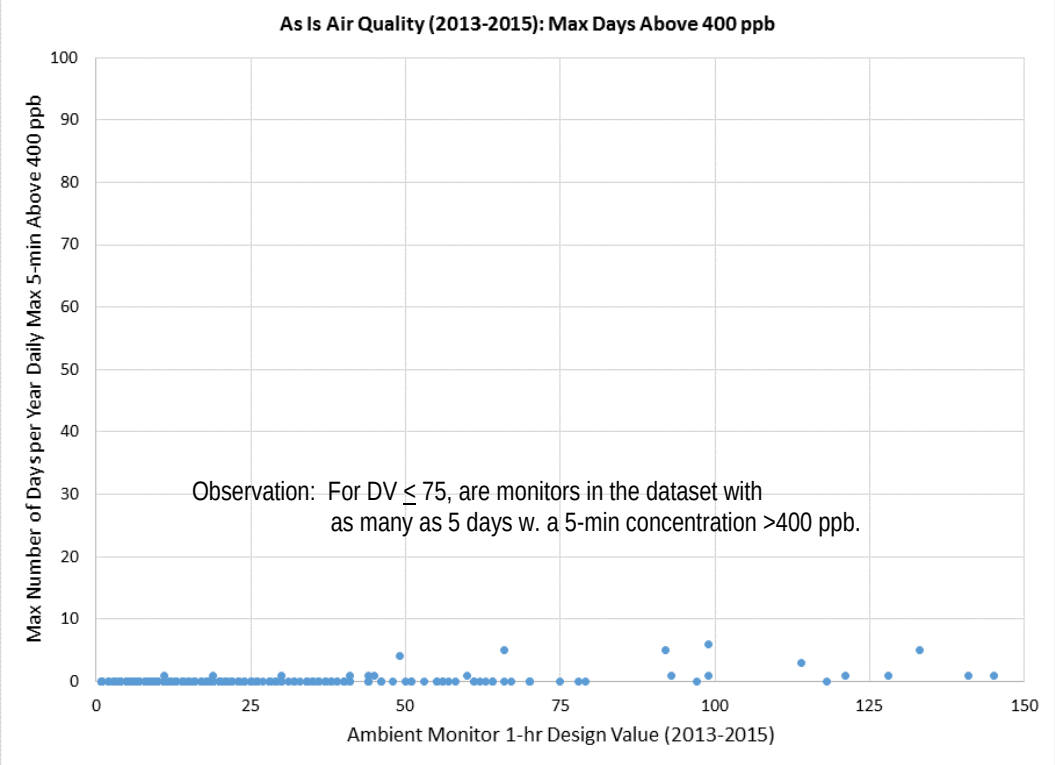
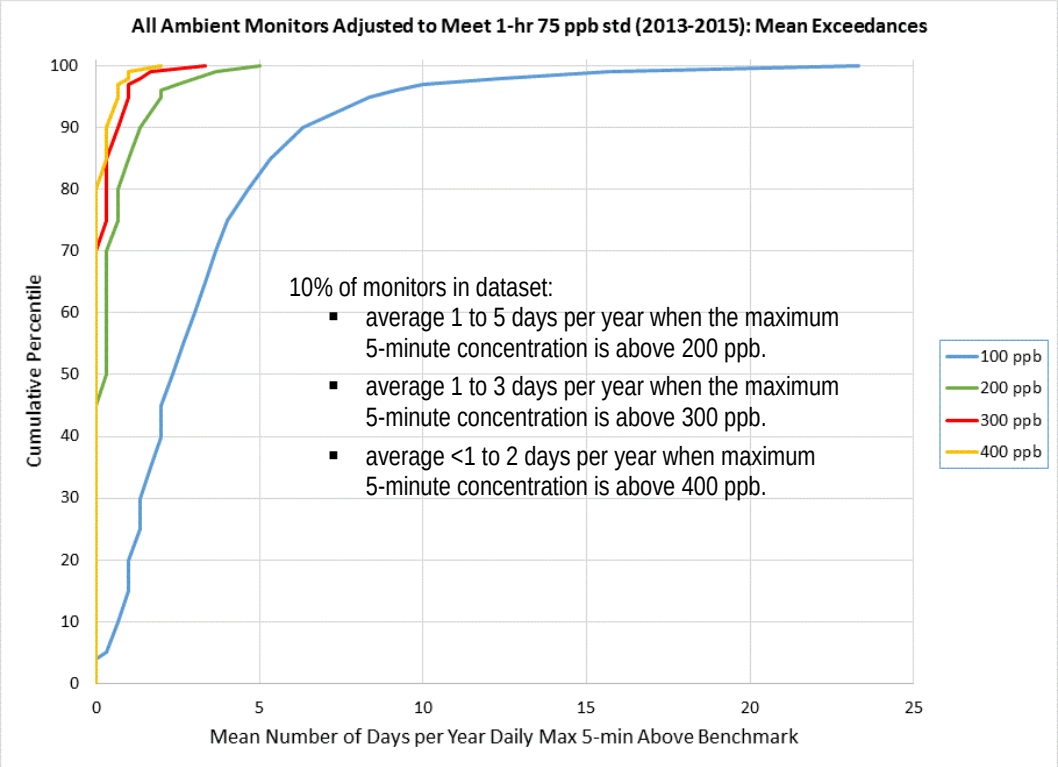
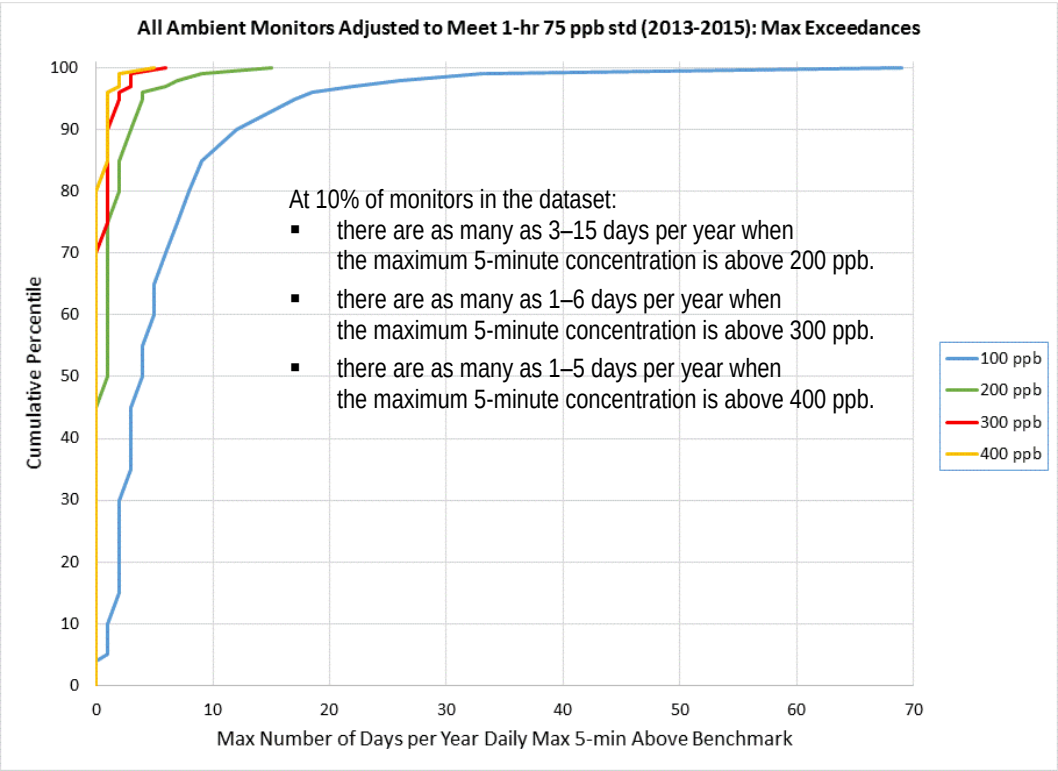


Figure B-5. Monitoring data (2013-2015) adjusted to just meet the current standard (75 ppb as a 3-year average of annual 99th percentile 1-hour daily maximum concentrations). Mean number of days/year (top panel) and maximum number of days/year (bottom panel) with daily maximum 5-minute concentrations of SO_2 above 100, 200, 300 and 400 ppb.

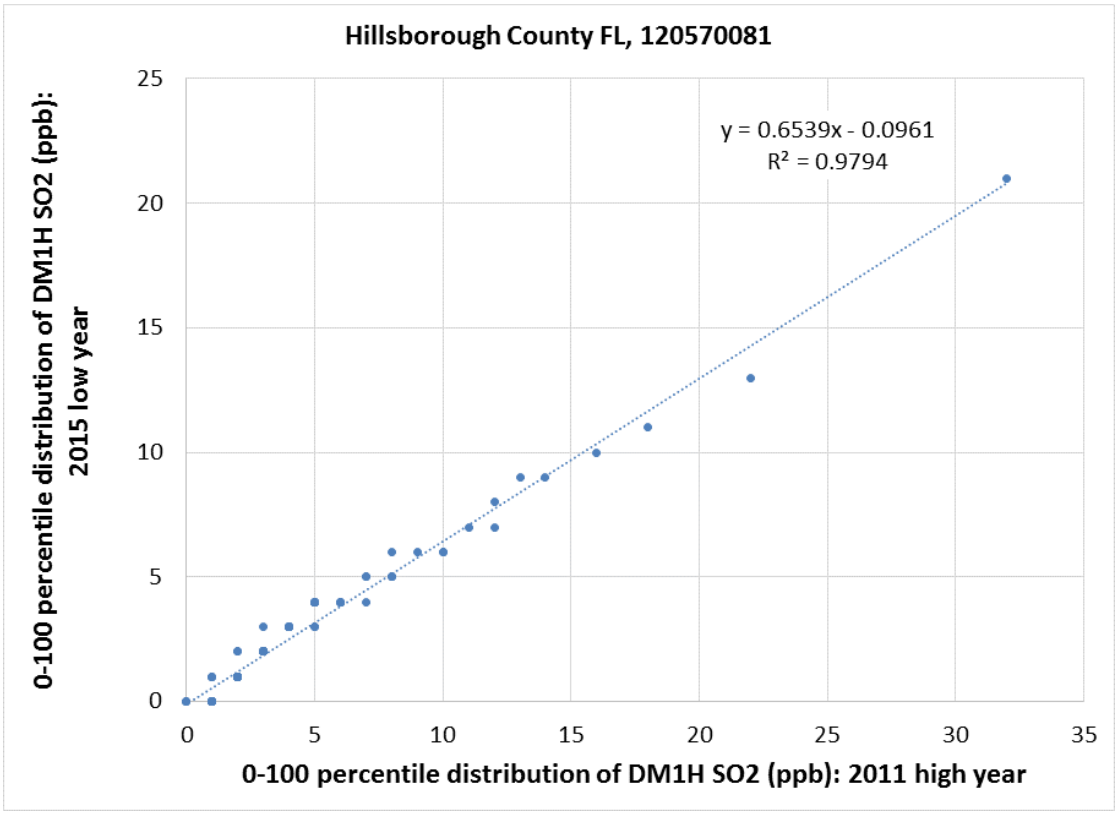


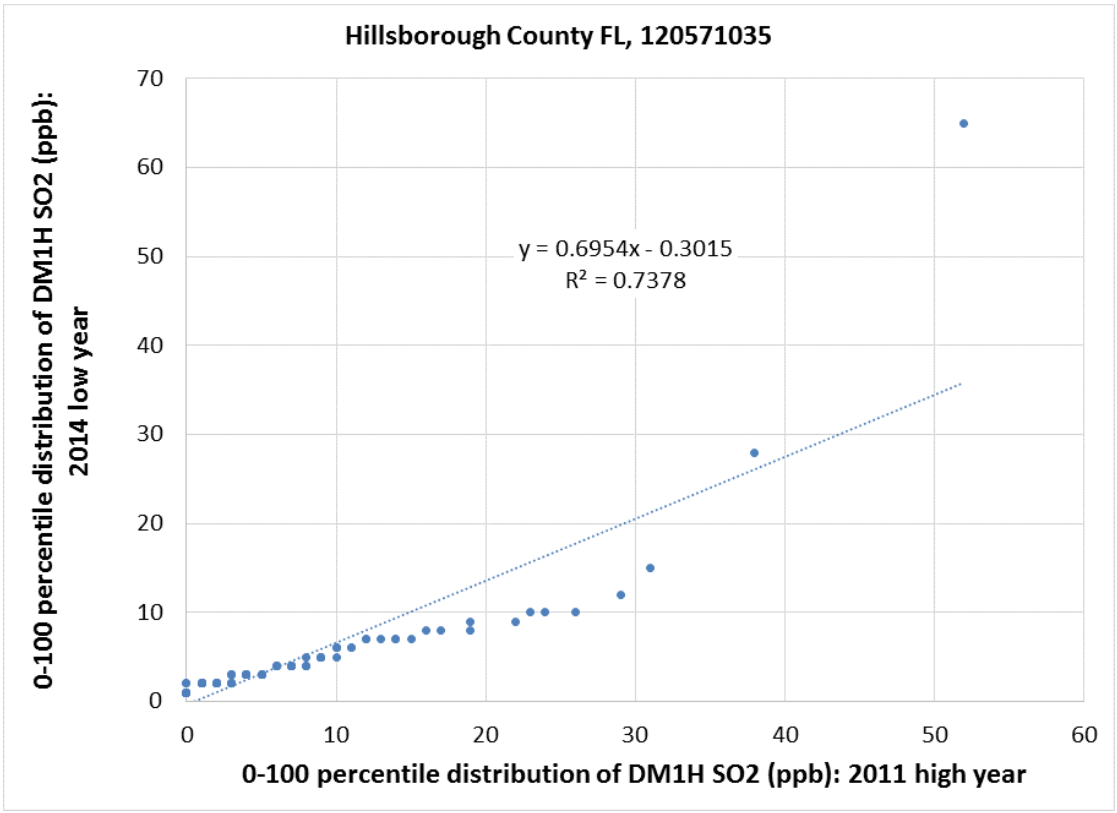


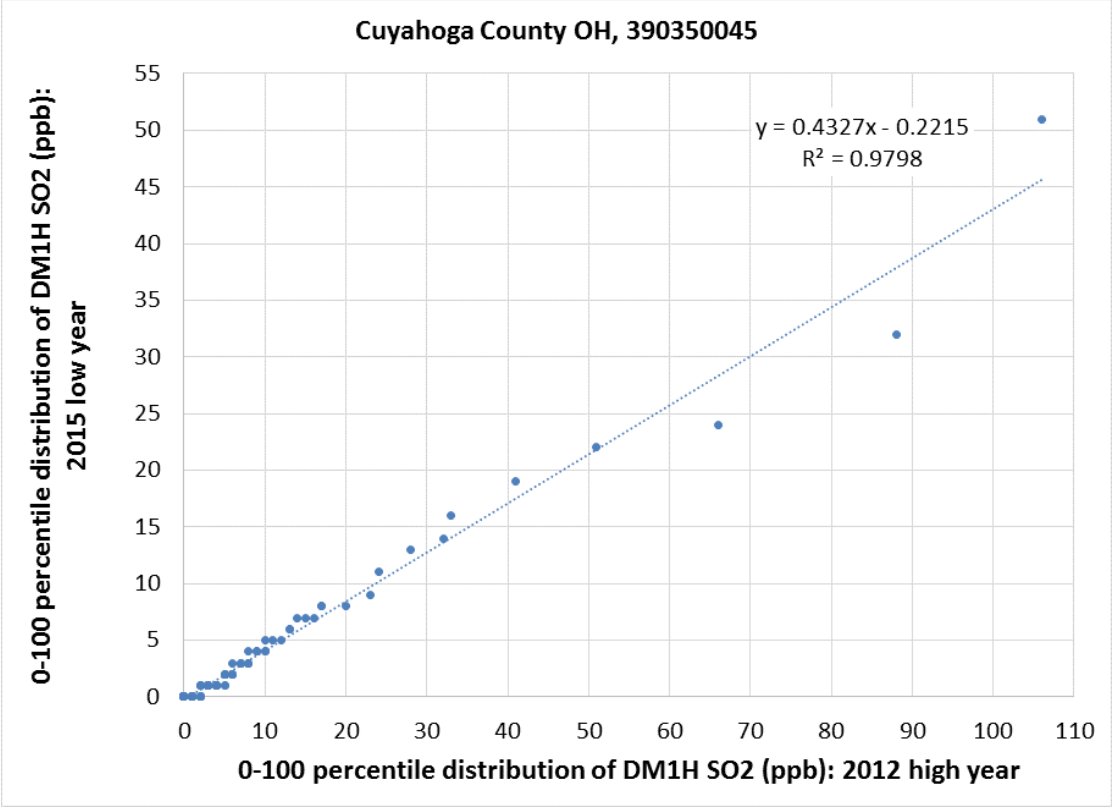
APPENDIX C. COMPARISONS OF SO_2 HOURLY CONCENTRATION DISTRIBUTIONS BETWEEN HIGH AND LOW YEARS IN 2011-2015

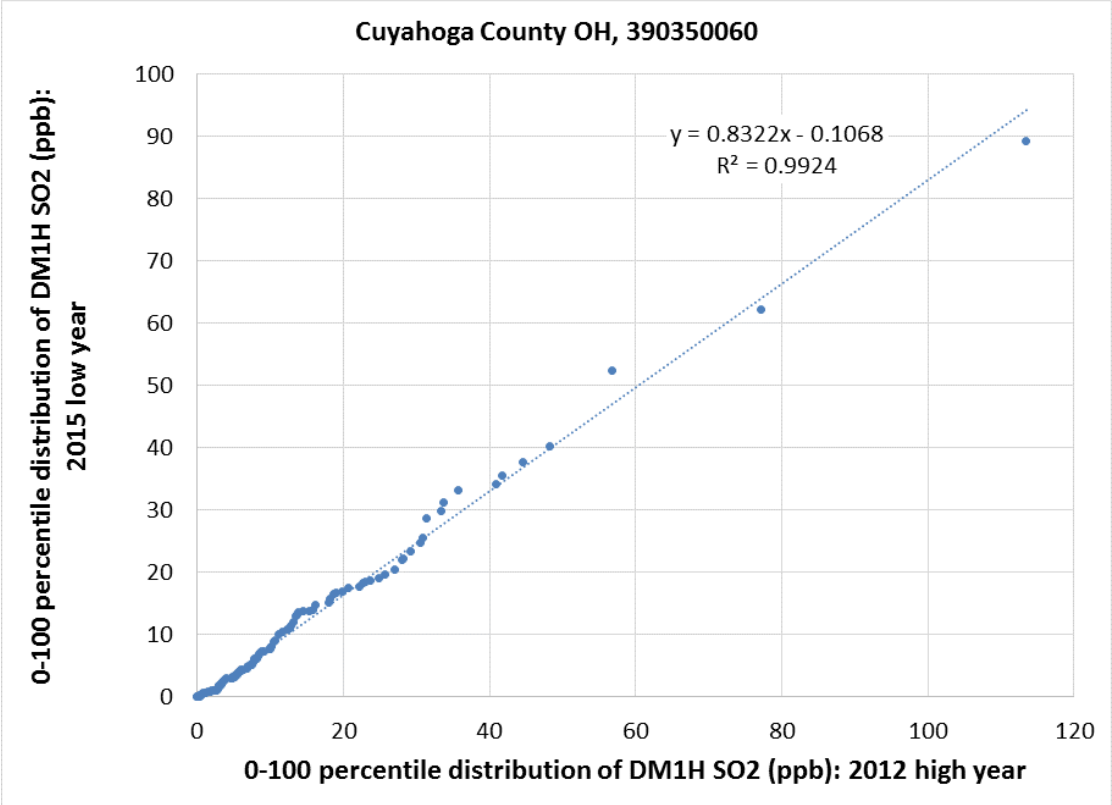
Preface: The figures included in this appendix illustrate preliminary analyses of air quality data for the years 2011-2015.

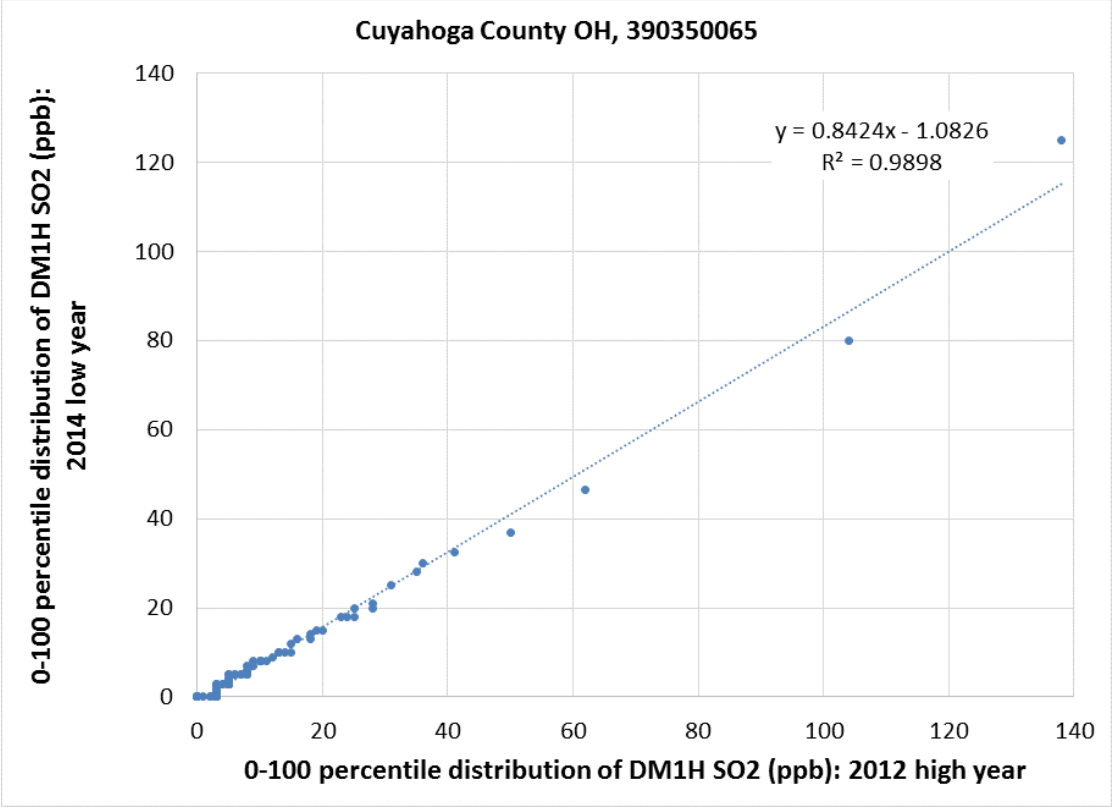
The figures below represent the analyses of recent air quality data to evaluate the appropriateness of the proportional adjustment approach used in the 2009 REA. As described in section 4.1.3.4, the figures below are the results for the monitors in the potential study areas that did not have the highest design value during the 2011-2015 period. The figures below compare the monitoring data for a low concentration year with a data for a high concentration year, with low and high defined by having a design value that is either below (a low year) or above (a high year) the level of the existing standard (99th percentile daily maximum 1-hour of 75 ppb).

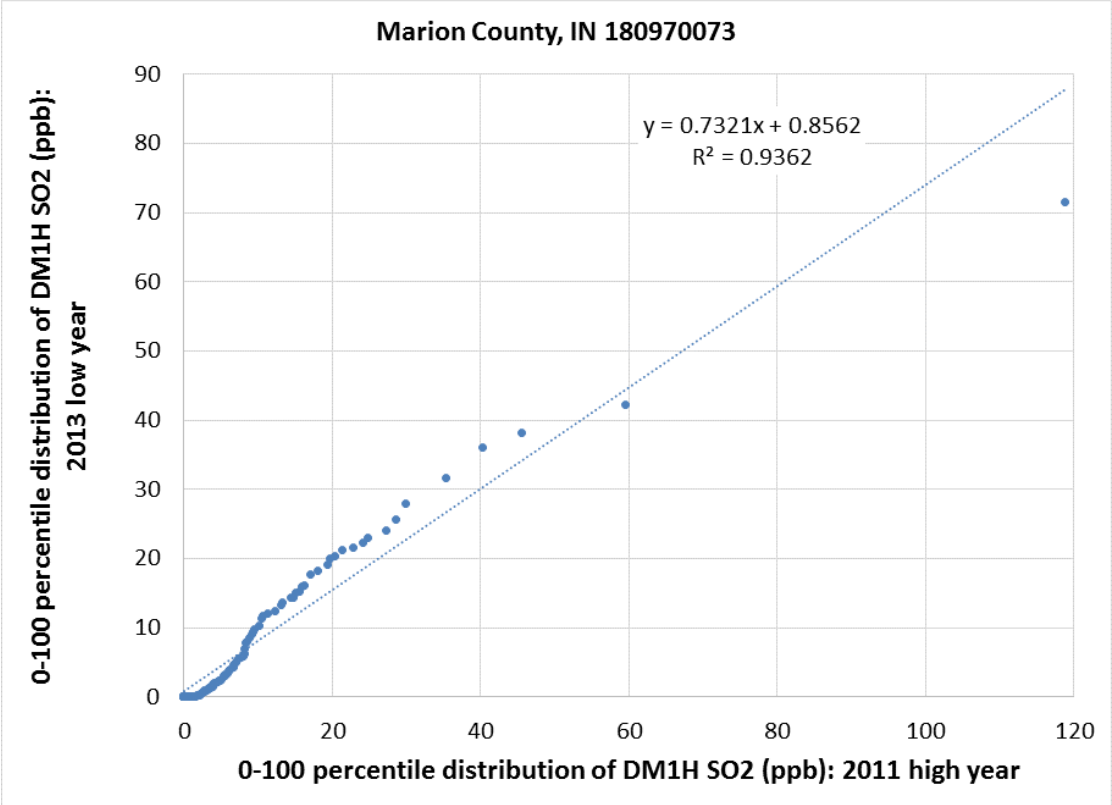

Hillsborough County FL, 120570081
y = 0.6539x - 0.0961
R² = 0.9794
0-100 percentile distribution of DM1H SO2 (ppb): 2015 low year
0-100 percentile distribution of DM1H SO2 (ppb): 2011 high year
0
5
10
15
20
25
30
35

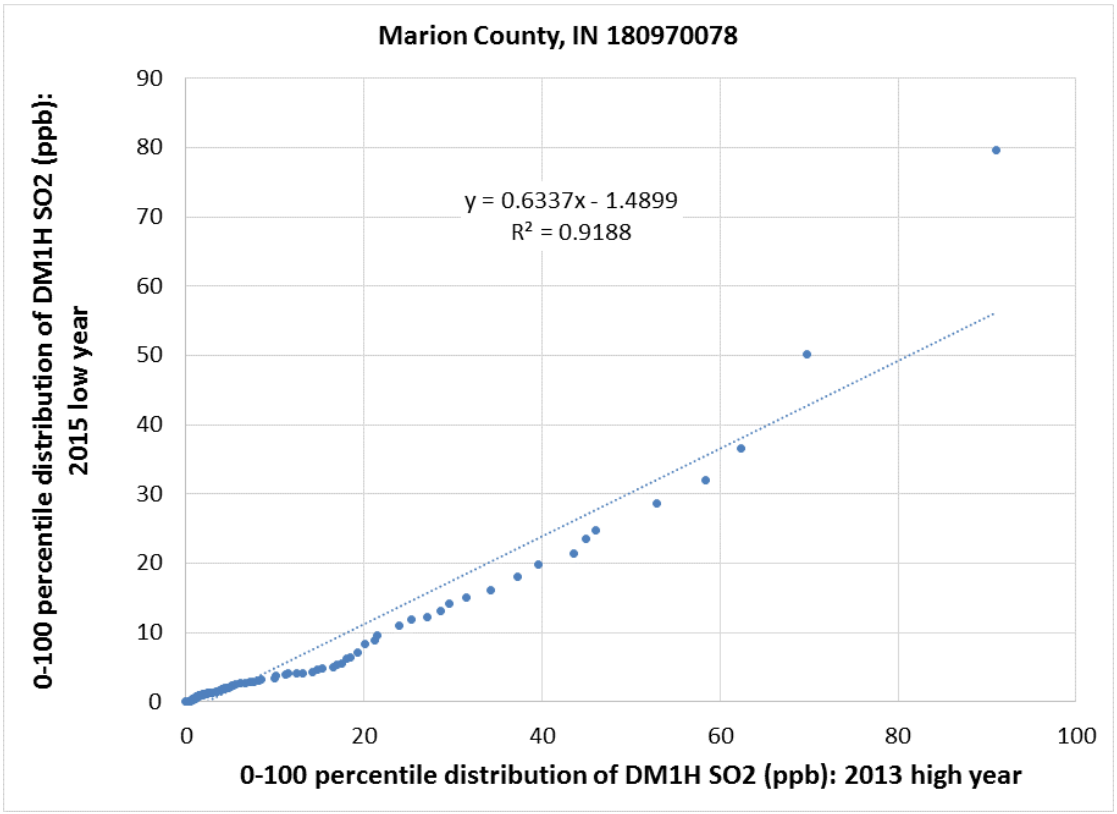

Hillsborough County FL, 120571035
y = 0.6954x - 0.3015
R² = 0.7378
0-100 percentile distribution of DM1H SO2 (ppb): 2014 low year
0-100 percentile distribution of DM1H SO2 (ppb): 2011 high year
0
10
20
30
40
50
60
70


Cuyahoga County OH, 390350045
y = 0.4327x - 0.2215
R² = 0.9798
0-100 percentile distribution of DM1H SO2 (ppb): 2015 low year
0-100 percentile distribution of DM1H SO2 (ppb): 2012 high year
0
5
10
15
20
25
30
35
40
45
50
55
0
10
20
30
40
50
60
70
80
90
100
110


Cuyahoga County OH, 390350060
y = 0.8322x - 0.1068
R² = 0.9924
0-100 percentile distribution of DM1H SO2 (ppb): 2015 low year
0-100 percentile distribution of DM1H SO2 (ppb): 2012 high year
0
10
20
30
40
50
60
70
80
90
100
0
20
40
60
80
100
120


Cuyahoga County OH, 390350065
y = 0.8424x - 1.0826
R² = 0.9898
0-100 percentile distribution of DM1H SO2 (ppb): 2014 low year
0-100 percentile distribution of DM1H SO2 (ppb): 2012 high year
0
20
40
60
80
100
120
140


Marion County, IN 180970073
y = 0.7321x + 0.8562
R² = 0.9362
0-100 percentile distribution of DM1H SO2 (ppb): 2013 low year
0-100 percentile distribution of DM1H SO2 (ppb): 2011 high year
0
10
20
30
40
50
60
70
80
90
100
120


Marion County, IN 180970078
y = 0.6337x - 1.4899
R² = 0.9188
0-100 percentile distribution of DM1H SO2 (ppb): 2015 low year
0-100 percentile distribution of DM1H SO2 (ppb): 2013 high year
0
10
20
30
40
50
60
70
80
90
0
20
40
60
80
100

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