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Ozone National Ambient Air Quality Standards: Scope and Methods Plan for Health Risk and Exposure Assessment

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Office of Air Quality Planning and Standards
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U.S. Environmental Protection Agency
Office of Air and Radiation
Office of Air Quality Planning and Standards
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List of Acronyms/Abbreviations

Act	Clean Air Act
AHRQ	Agency for Healthcare Research and Quality
APEX	EPA's Air Pollutants Exposure model, version 4
AQS	EPA's Air Quality System
BenMAP	Benefits Mapping Analysis Program
CASAC	Clean Air Scientific Advisory Committee
CHAD	EPA's Consolidated Human Activity Database
CONUS	Continental United States
C-R	Concentration-response relationship
CSA	Consolidated Statistical Area
CTM	Chemical transport models
EPA	United States Environmental Protection Agency
FEM	Federal Equivalent Method
FIP	Federal Implementation Plan
FRM	Federal Reference Method
ISA	Integrated Science Assessment
NAAQS	National Ambient Air Quality Standards
NAPS	National Air Pollution Surveillance
NCEA	National Center for Environmental Assessment
NEI	National Emissions Inventory
NERL	National Exposure Research Laboratory
NCDC	National Climatic Data Center
NCore	National Core Monitoring Network
NOx	Nitrogen oxides
O_3	Ozone
OAQPS	Office of Air Quality Planning and Standards
OAR	Office of Air and Radiation
OMB	Office of Management and Budget
ORD	Office of Research and Development
PRB	Policy-Relevant Background
QA	Quality assurance
QC	Quality control
RR	Relative risk
SAB	Science Advisory Board
REA	Risk and Exposure Assessment
SEDD	State Emergency Department Databases
SID	State Inpatient Database
SO_2	Sulfur Dioxide
SO_x	Sulfur Oxides
TSP	Total suspended particulate
VOC	Volatile organic compounds

1 INTRODUCTION

The U.S. Environmental Protection Agency (EPA) is presently conducting a review of the national ambient air quality standards (NAAQS) for ozone. Sections 108 and 109 of the Clean Air Act (Act) govern the establishment and periodic review of the NAAQS. These standards are established for pollutants that may reasonably be anticipated to endanger public health and welfare, and whose presence in the ambient air results from numerous or diverse mobile or stationary sources. The NAAQS are to be based on air quality criteria, which are to accurately reflect the latest scientific knowledge useful in indicating the kind and extent of identifiable effects on public health or welfare that may be expected from the presence of the pollutant in ambient air. The EPA Administrator is to promulgate and periodically review, at five-year intervals, "primary" (health-based) and "secondary" (welfare-based) NAAQS for such pollutants.[1] 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 Act also requires that an independent scientific review committee advise the Administrator as part of this NAAQS review process, a function now performed by the Clean Air Scientific Advisory Committee (CASAC).

EPA's overall plan and schedule for this ozone NAAQS review are presented in the *Integrated Review Plan for the Ozone National Ambient Air Quality Standards Review* (U.S. EPA, 2011a). That plan outlines the Clean Air Act (CAA) requirements related to the establishment and reviews of the NAAQS, the process and schedule for conducting the current ozone NAAQS review, and two key components in the NAAQS review process: an *Integrated Science Assessment* (ISA) and a *Risk and Exposure Assessment* (REA). It also lays out the key policy-relevant issues to be addressed in this review as a series of policy-relevant questions that will frame our approach to determining whether the current primary and secondary NAAQS for ozone should be retained or revised.

[1]Section 109(b)(1) [42 U.S.C. 7409] of the Act 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."

The ISA prepared by EPA's Office of Research and Development (ORD), National Center for Environmental Assessment (NCEA), provides a critical assessment of the latest available policy-relevant scientific information upon which the NAAQS are to be based. The ISA will critically evaluate and integrate scientific information on the health and welfare effects associated with exposure to ozone in the ambient air. The REA, prepared by EPA's Office of Air and Radiation (OAR), Office of Air Quality Planning and Standards (OAQPS), will draw from the information assessed in the ISA. The REA will include, as appropriate, quantitative estimates of human and ecological exposures and/or risks associated with recent ambient levels of ozone, with levels simulated to just meet the current standards, and with levels simulated to just meet possible alternative standards.

The REA will be developed in two parts addressing: (1) human health risk and exposure assessment and (2) other welfare-related effects assessment. This document describes the scope and methods planned to conduct the human health risk and exposure assessments to support the review of the primary (health-based) ozone NAAQS. A separate document describes the scope and methods planned to conduct quantitative assessments to support the review of the secondary (welfare-based) ozone NAAQS. Preparation of these two planning documents coincides with the development of the first draft ozone ISA (U.S. EPA, 2011b) to facilitate the integration of policy-relevant science into all three documents.

This planning document is intended to provide enough specificity to facilitate consultation with CASAC, as well as for public review, in order to obtain advice on the overall scope, approaches, and key issues in advance of the conduct of the risk and exposure analyses and presentation of results in the first draft REA. NCEA has compiled and assessed the latest available policy-relevant science available to produce a first draft of the ISA (U.S. EPA, 2011b). The first draft ISA has been reviewed by staff and used in the development of the approaches described below. This includes information on source emissions, atmospheric chemistry, air quality, human exposure, and related health effects. CASAC consultation on this planning document coincides with its review of the first draft ISA. CASAC and public comments on this document will be taken into consideration in the development of the first draft REA, the preparation of which will coincide with and draw from the second draft ISA. The second draft

REA will draw on the final ISA and will reflect consideration of CASAC and public comments on the first draft REA. The final REA will reflect consideration of CASAC and public comments on the second draft REA. The final ISA and final REA will inform the policy assessment and rulemaking steps that will lead to a final decision on the ozone NAAQS.

This introductory chapter includes background on the current ozone standards and the quantitative risk assessment conducted for the last review; the key issues related to designing the quantitative assessments in this review, building upon the lessons learned in the last review; and an overview introducing the planned assessments that are described in more detail in later chapters. The planned assessments are designed to estimate human exposures and/or health risks that are associated with recent ambient levels, with ambient levels simulated to just meet the current standards, and with ambient levels simulated to just meet alternative standards that may be considered. The major components of the assessments (e.g., air quality analyses, quantitative exposure assessment, and quantitative health risk assessments) briefly outlined in the Integrated Review Plan (U.S. EPA, 2011a), are conceptually presented in Figure 1-1, and are described in more detail below in Chapters 2 – 6. The schedule for completing these assessments is presented in Chapter 7.

1.1 Background on Last Ozone NAAQS Review

As a first step in developing this planning document, we considered the work completed in previous reviews of the primary NAAQS for ozone (U.S. EPA, 2011a, see section 1.3) and in particular the quantitative assessments supporting those reviews. EPA completed the most recent review of the ozone NAAQS with publication of a decision on March 27, 2008 (73 FR 16436). Based on the final CD (U.S. EPA, 2006) published in March of 2006, and on the final Staff Paper (U.S EPA, 2007a) published in July of 2007, the previous EPA Administrator decided to revise the level of the 8-hour primary ozone standard from 0.08 ppm to 0.075 ppm and to revise the secondary to be identical to the primary. As discussed in more detail in the Integrated Review Plan, the current EPA Administrator has decided to reconsider the March 27, 2008 decisions on the revisions to the primary and secondary ozone NAAQS.

1.1.1 Overview of Exposure Assessment for Ozone from Last Review

The exposure and health risk assessment conducted in the review completed in March 2008 developed exposure and health risk estimates for 12 urban areas across the U.S., which were chosen, based on the location of ozone epidemiological studies and to represent a range of geographic areas, population demographics, and ozone climatology. That analysis was in part based upon the exposure and health risk assessments done as part of the review completed in 1997.[1] The exposure and risk assessment incorporated air quality data (i.e., 2002 through 2004) and provided annual or ozone season-specific exposure and risk estimates for these recent years of air quality and for air quality scenarios simulating just meeting the existing 8-hour ozone standard and several alternative 8-hour ozone standards. Exposure estimates were used as an input to the risk assessment for lung function responses (a health endpoint for which exposure-response functions were available from controlled human exposure studies). Exposure estimates were developed for the general population and population groups including school age children with asthma as well as all school age children. The exposure estimates also provided information on population exposures exceeding potential health effect benchmark levels that were identified based on the observed occurrence of health endpoints not explicitly modeled in the health risk assessment (e.g., lung inflammation, increased airway responsiveness, and decreased resistance to infection) associated with 6-8 hour exposures to ozone in controlled human exposure studies.

The exposure analysis took into account several important factors including the magnitude and duration of exposures, frequency of repeated high exposures, and breathing rate of individuals at the time of exposure. Estimates were developed for several indicators of exposure to various levels of ozone air quality, including counts of people exposed one or more times to a given ozone concentration while at a specified breathing rate, and counts of person-occurrences which accumulate occurrences of specific exposure conditions over all people in the population groups of interest over an ozone season.

1 In the 1994-1997 Ozone NAAQS review, EPA conducted exposure analyses for the general population, children who spent more time outdoors, and outdoor workers. Exposure estimates were generated for 9 urban areas for "as is" air quality and for just meeting the existing 1-hour standard and several alternative 8-hour standards. Several reports (Johnson et al., 1996a,b,c) that describe these analyses can be found at: http://www.epa.gov/ttn/naaqs/standards/ozone/s_o3_pr.html.

As discussed in the 2007 Staff Paper and in Section IIa of the ozone Final Rule (73 FR 16440 to 16442, March 27, 2008), the most important uncertainties affecting the exposure estimates were related to modeling human activity patterns over an ozone season, modeling of variations in ambient concentrations near roadways, and modeling of air exchange rates that affect the amount of ozone that penetrates indoors. Another important uncertainty, discussed in more detail in the Staff Paper (section 4.3.4.7), was the uncertainty in energy expenditure values which directly affected the modeled breathing rates. These were important since they were used to classify exposures occurring when children were engaged in moderate or greater exertion and health effects observed in the controlled human exposure studies generally occurred under these exertion levels for 6 to 8-hour exposures to ozone concentrations at or near 0.08 ppm. Reports that describe these analyses (U.S. EPA, 2007a,b; Langstaff, 2007) can be found at: http://www.epa.gov/ttn/naaqs/standards/ozone/s_o3_index.html.

1.1.2 Overview of Health Risk Assessment for Ozone from Last Review

The human health risk assessment presented in the review completed in March 2008 was designed to estimate population risks in a number of urban areas across the U.S., consistent with the scope of the exposure analysis described above. The risk assessment included risk estimates based on both controlled human exposure studies and epidemiological and field studies. Ozone-related risk estimates for lung function decrements were generated using probabilistic exposure-response relationships based on data from controlled human exposure studies, together with probabilistic exposure estimates from the exposure analysis. For several other health endpoints, ozone-related risk estimates were generated using concentration-response relationships reported in epidemiological or field studies, together with ambient air quality concentrations, baseline health incidence rates, and population data for the various locations included in the assessment. Health endpoints included in the assessment based on epidemiological or field studies included: hospital admissions for respiratory illness in four urban areas, premature mortality in 12 urban areas, and respiratory symptoms in asthmatic children in 1 urban area.

In the health risk assessment conducted in the previous review, EPA recognized that there were many sources of uncertainty and variability in the inputs to the assessment and that there

was a high degree of uncertainty in the resulting risk estimates. The statistical uncertainty surrounding the estimated ozone coefficients in concentration-response functions as well as the shape of the exposure-response relationship chosen were addressed quantitatively. Additional uncertainties were addressed through sensitivity analyses and/or qualitatively. The risk assessment conducted for that ozone NAAQS review incorporated some of the variability in key inputs to the assessment by using location-specific inputs (e.g., location-specific concentration-response function, baseline incidence rates and population data, and air quality data for epidemiological–based endpoints, location specific air quality data and exposure estimates for the lung function risk assessment). In that review, several urban areas were included in the health risk assessment to provide some sense of the variability in the risk estimates across the U.S.

Key observations and insights from the ozone risk assessment, in addition to important caveats and limitations, were addressed in Section II.B of the Final Rule notice (73 FR 16440 to 16443, March 27, 2008). In general, estimated risk reductions associated with going from current ozone levels to just meeting the current and alternative 8-hour standards showed patterns of decreasing estimated risk associated with just meeting the lower alternative 8-hour standards considered. Furthermore, the estimated percentage reductions in risk were strongly influenced by the baseline air quality year used in the analysis, which was due to significant year-to-year variability in ozone concentrations. There was also noticeable city-to-city variability in the estimated ozone-related incidence of morbidity and mortality across the 12 urban areas. Uncertainties associated with estimated policy-relevant background (PRB) concentrations[1] were also addressed and revealed differential impacts on the risk estimates depending on the health effect considered as well as the location. EPA also acknowledged that there were considerable uncertainties surrounding estimates of ozone coefficients and the shape for concentration-response relationships and whether or not a population threshold or non-linear relationship exists within the range of concentrations examined in the epidemiological studies.

1 For the purposes of the risk and exposure assessments, policy-relevant background (PRB) ozone has been defined in previous reviews as the distribution of ozone concentrations that would be observed in the U.S. in the absence of anthropogenic (man-made) emissions of ozone precursor emissions (e.g., VOC, CO, NO_x) in the U.S., Canada, and Mexico.

1.2 Goals for Framing the Assessments in the Current Review

A critical step in designing the quantitative risk and exposure assessments is to clearly identify the policy-relevant questions to be addressed by these assessments. As identified above, the Integrated Review Plan presents a series of key policy questions (U.S. EPA, 2011a, section 3.1). To answer these questions, EPA will integrate information from the ISA and from air quality, risk, and exposure assessments as we evaluate both evidence-based and risk-based considerations.

More specifically, to focus the REA, we have identified the following goals for the exposure and risk assessment: (1) to provide estimates of the number of people in the general population and in sensitive populations with ozone exposures above benchmark levels; (2) to provide estimates of the number of people in the general population and in sensitive populations with impaired lung function resulting from exposures to ozone; (3) to provide estimates of the potential magnitude of premature mortality and/or selected morbidity health effects in the population, including sensitive populations, where data are available to assess these subgroups, associated with recent ambient levels of ozone and with just meeting the current suite of ozone standards and any alternative standards that might be considered in selected urban study areas; (4) to develop a better understanding of the influence of various inputs and assumptions on the risk estimates to more clearly differentiate alternative standards that might be considered including potential impacts on various sensitive populations; and (5) to gain insights into the distribution of risks and patterns of risk reduction and uncertainties in those risk estimates. In addition, we are considering conducting an assessment to provide nationwide estimates of the potential magnitude of premature mortality associated with ambient ozone exposures to more broadly characterize this risk on a national scale, to assess the extent to which we have captured the upper end of the risk distribution, and to support the interpretation of the more detailed risk results generated for the selected urban study areas.

1.3 Overview of Current Assessment Plan

This plan is designed to outline the scope and approaches and highlight key issues in the estimation of population exposures and health risks posed by ozone under existing air quality levels ("as is" exposures and health risks), upon attainment of the current ozone primary

NAAQS, and upon meeting various alternative standards in selected sample urban areas. This plan is intended to facilitate consultation with the CASAC, as well as public review, and to obtain advice on the overall scope, approaches, and key issues in advance of the completion of such analyses and presentation of results in the first draft of the ozone Policy Assessment.

The planned ozone exposure analysis and health risk assessment address short-term and long-term exposures to ozone and associated health effects. These assessments cover a variety of health effects for which there is adequate information to develop quantitative risk estimates. However, there are some health endpoints for which there currently is insufficient information to develop quantitative risk estimates. Staff plans to discuss these additional health endpoints qualitatively in the ozone Policy Assessment. The risk assessment is intended as a tool that, together with other information on these health endpoints and other health effects evaluated in the ozone ISA and ozone Policy Assessment, can aid the Administrator in judging whether the current primary standard is requisite to protect public health with an adequate margin of safety, or whether revisions to the standard are appropriate.

Staff plans to perform exposure and health risk analyses using the three most recent years of air quality data available at this time, 2008-2010. The time period to be analyzed will be the ozone season, which in the urban areas to be included in this assessment, varies from April to October to the entire year depending on the region of the country.

1.3.1 Air Quality Assessment

Chapter 2 describes assessments planned for the current review of the primary NAAQS for ozone including air quality analyses to be conducted to support quantitative risk and exposure assessments in selected urban study areas as well as to support evidence-based considerations and to place the results of the quantitative assessments into a broader public health perspective. Air quality inputs will include: (1) recent air quality data for ozone from suitable monitors for each selected urban study area; (2) estimates of background concentrations for each selected urban study area, and (3) simulated air quality that reflects changes in the distribution of ozone air quality estimated to occur when an area just meets the current or alternative ozone standards under consideration.

1.3.2 Exposure Assessment

Chapter 3 discusses our plan to conduct a quantitative exposure assessment in this review. The exposure assessment will build upon the methodology, analyses, and lessons learned from assessments conducted for other recent NAAQS reviews. EPA plans to model population exposures to ambient ozone in three or more of the 12 urban areas modeled in the previous review (Atlanta, Boston, Chicago, Cleveland, Detroit, Houston, Los Angeles, New York, Philadelphia, Sacramento, St. Louis, and Washington D.C.), as well as a high-elevation area such as Denver. The number of areas modeled will depend on the available resources. These areas were selected to be generally representative of a variety of populations, geographic areas, climates, and different ozone and co-pollutant levels, and are areas where epidemiologic studies have been conducted that are planned to be used to support the quantitative risk assessment. In addition to providing population exposures for estimation of lung function effects, the exposure modeling will provide a characterization of urban air pollution exposure environments and activities resulting in the highest exposures, differences in which may partially explain the heterogeneity across urban areas seen in the risks associated with ozone air pollution.

1.3.3 Health Risk Assessment

The health risk assessment will estimate various health effects associated with ozone exposures for current ozone levels, based on 2008-2010 air quality data, as well as reductions in risk associated with attaining the current 8-hour ozone NAAQS and alternative ozone standards, based on adjusting 2008-2010 air quality data. Risk estimates will be developed for several urban areas located throughout the U.S., including the areas for which exposure modeling will be performed. Health endpoints to be examined in the risk assessment include: lung function decrements, respiratory symptoms in asthmatic children, school absences, emergency department visits for respiratory causes, respiratory- and cardiac-related hospital admissions, and mortality.

At this time, two general types of human studies are particularly relevant for deriving quantitative relationships between ozone levels and human health effects: (1) controlled human exposure studies and (2) epidemiological and field studies. Controlled human exposure studies involve volunteer subjects who are exposed while engaged in different exercise regimens to specified levels of ozone under controlled conditions for specified amounts of time. The

responses measured in such studies have included measures of lung function, such as forced expiratory volume in one second (FEV_1), respiratory symptoms, airway hyper-responsiveness, and inflammation. Prior EPA risk assessments for ozone have included risk estimates for lung function decrements and respiratory symptoms based on analysis of individual data from controlled human exposure studies. For the current health risk assessment, staff plans to use the probabilistic exposure-response relationships which were based on analyses of individual data that describe the relationship between a measure of personal exposure to ozone and the measure(s) of lung function recorded in the study. The measure of personal exposure to ambient ozone is typically some function of hourly exposures – e.g., 1-hour maximum or 8-hour maximum. Therefore, a risk assessment based on exposure-response relationships derived from controlled human exposure study data requires estimates of personal exposure to ozone, typically on a 1-hour or multi-hour basis. Because data on personal hourly ozone exposures are not available, estimates of personal exposures to varying ambient concentrations are derived through exposure modeling, as described in Chapter 3.

The risk assessment based on controlled human exposure studies is described in Chapter 4. In contrast to the **exposure-response** relationships derived from controlled human exposure studies, epidemiological and field studies provide estimated **concentration-response** relationships based on data collected in real world settings. Ambient ozone concentration is typically measured as the average of monitor-specific measurements, using population-oriented monitors. Population health responses for ozone have included population counts of school absences, emergency room visits, hospital admissions for respiratory and cardiac illness, respiratory symptoms, and premature mortality. As described more fully below in Chapter 5 and outlined in Figure 1-1, a risk assessment based on epidemiological studies typically requires baseline incidence rates and population data for the risk assessment locations.

The characteristics that are relevant to the planning and structure of a risk assessment based on controlled human exposure studies versus one based on epidemiology or field studies can be summarized as follows:

- A risk assessment based on controlled human exposure studies uses exposure-response functions, and thus requires estimates of personal exposures. It therefore

involves an exposure modeling step that is not needed in a risk assessment based on epidemiology or field studies, which uses concentration-response functions.

- Epidemiological and field studies are carried out in specific real world locations (e.g., specific urban areas). To minimize uncertainty, a risk assessment based on epidemiological studies can be performed for the locations in which the studies were carried out. Controlled human exposure studies, carried out in laboratory settings, are generally not specific to any particular real world location. A controlled human exposure studies-based risk assessment can therefore appropriately be carried out for any locations for which there are adequate air quality data on which to base the modeling of personal exposures. There are, therefore, some locations for which a controlled human exposure studies-based risk assessment could appropriately be carried out but an epidemiological studies-based risk assessment could not, according to our criteria for city selection.

- The adequate modeling of hourly personal exposures associated with ambient concentrations requires more complete ambient monitoring data than are necessary to estimate average ambient concentrations used to calculate risks based on concentration-response relationships. Therefore, there may be some locations in which an epidemiological studies-based risk assessment could appropriately be carried out but a controlled human exposure studies-based risk assessment would have increased uncertainty.

- To derive estimates of risk or risk reduction from concentration-response relationships estimated in epidemiological studies, it is usually necessary to have estimates of the baseline incidences of the health effects involved. Such baseline incidence estimates are not needed in a controlled human exposure studies-based risk assessment.

Overviews of the scope and methods for each type of risk assessment are discussed in Chapters 4 and 5 below.

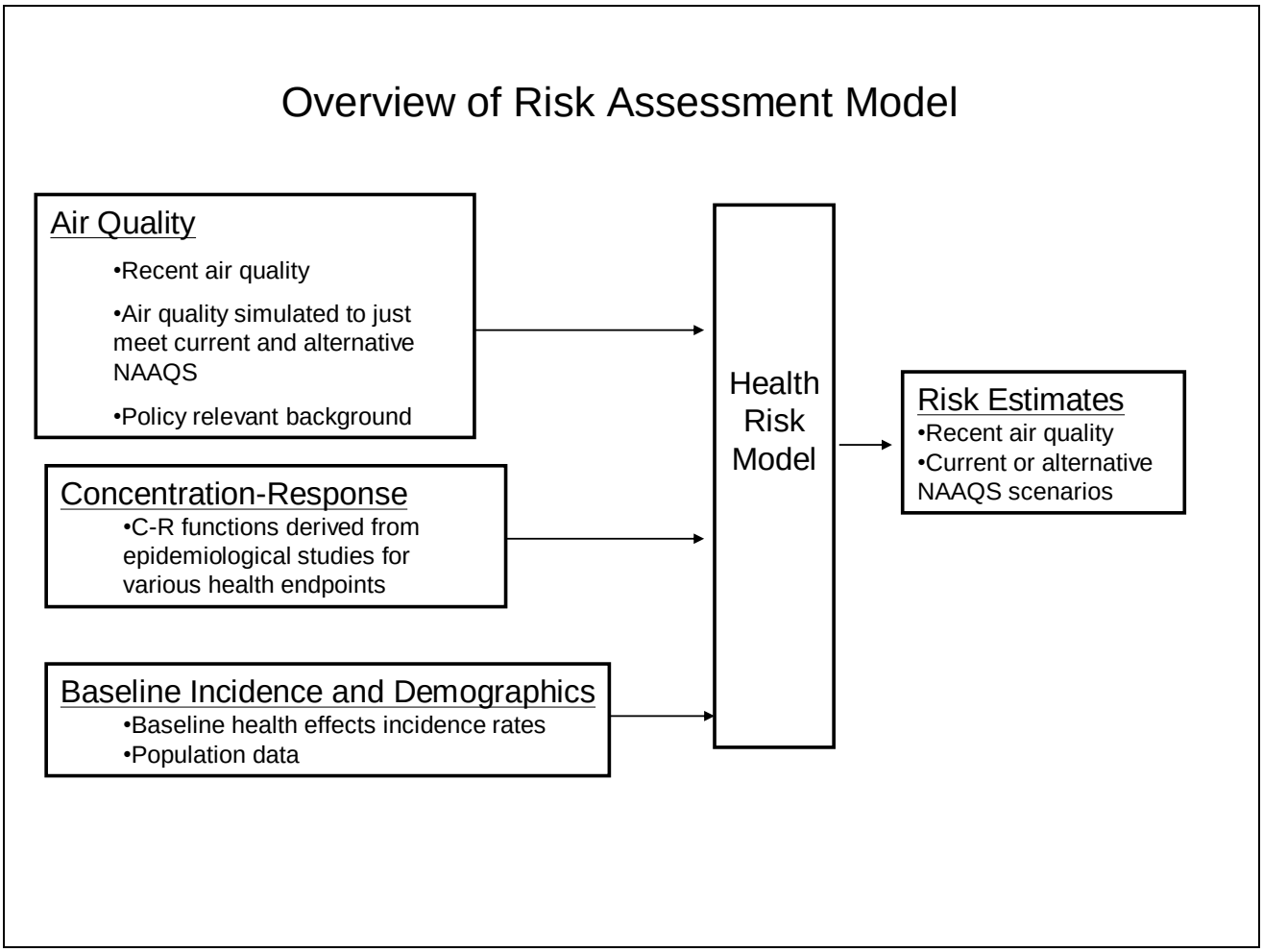


Figure 1-1. Overview of Risk Assessment Based on Epidemiologic Studies

2 AIR QUALITY CONSIDERATIONS

2.1 Introduction

A number of air quality analyses are planned to provide inputs for the risk and exposure assessments that will be conducted for selected urban study areas as well as to provide a broader understanding of ozone air quality, in order to inform: (1) evidence-based considerations; (2) our understanding of the risk and exposure assessment results to better characterize potential nationwide public health impacts associated with exposures to ozone; and (3) policy considerations related to evaluating possible alternative NAAQS. Specific goals for the planned air quality assessments include:

- Characterizing air quality in various locations across the U.S. in terms of ozone considering differences in ozone ambient concentrations, and spatial and temporal patterns to help inform the selection of specific cities that we plan to include in the risk and exposure assessments.
- Characterizing background concentrations of ozone based on chemical transport modeling (U.S. EPA, 2011b, section 3.4).
- Providing air quality distributions for ozone for a number of alternative scenarios in the selected urban study areas including:
    - Recent air quality;
    - Simulation of air quality to just meet the current primary standard; and
    - Simulation of air quality to just meet potential alternative primary standards for ozone under consideration.
- Providing a broader characterization of current ozone concentrations nationally (beyond the locations evaluated in the risk and exposure assessments).

2.2 Air Quality Inputs to Risk and Exposure Assessments

Important inputs to the ozone risk and exposure assessments are ambient ozone air quality data. For these assessments, EPA plans to use 2008-2010 air quality data obtained from EPA's Air Quality System (AQS), as these are the most recent data available.

2.2.1 Recent Air Quality

For ozone, in general, only data collected by Federal reference or equivalent methods (FRMs or FEMs) will be used in the risk and exposure assessments, consistent with the use of

such data in most of the health effects studies. However, if an epidemiologic study used non-FRM/FEM data from ozone monitors in a concentration-response function, consideration will be given to using the same type of data in the quantitative risk assessment for the same location. In order to be consistent with the approach generally used in the epidemiological studies that used estimated ozone concentration-response (C-R) functions for short-term effects, we plan to average ambient ozone concentrations on each day for which measured data are available for estimating health effects associated with 24-hour ambient concentrations. If epidemiologic studies used a composite monitor, then we will consider developing a data set for each assessment location based on a composite of all monitors according to the method in the epidemiologic study. As in the last review, some monitoring sites may be omitted, if needed, to best match the set of monitors that were used in the epidemiological studies.

In addition to matching our characterization of air quality at each assessment location to the approach from the epidemiological study used in modeling risk, we will also consider alternative approaches for characterizing air quality, if they produce estimates of exposure that are potentially more representative for the populations being assessed (even if they do not match the approach used in the epidemiology studies). For example, we may consider the use of monitor data (as described above) fused with photochemical modeling results for ozone. With this approach, we would use the monitor data to characterize absolute ozone levels across the urban study area (subject to the limitations of the monitoring framework's coverage) with the modeled results used to fill in the spatial pattern or gradient between monitors. We may also consider alternative approaches for generating composite monitor estimates that do not rely on modeling. For example, given the potential importance of commuting and workplace exposure in driving overall exposure profiles, we might consider generating composite monitor estimates that weight each monitor by "population exposure" (e.g., the person-hours of exposure associated with the immediate area surrounding a given monitor). With this approach, we would use the results of micro-environmental exposure modeling to estimate the amount of time that a simulated population spends in the vicinity of each monitor (see Section 5.2.2 for additional detail on these alternative approaches being considered for assessing current exposure).

Important factors to consider in deciding how to characterize current ambient ozone levels include the degree of spatial and temporal heterogeneity in monitored levels seen within a given assessment location. As part of planning for the analysis, we will consider trends in spatial and temporal gradients across ozone monitor data in the urban study areas we are considering.

2.2.2 Air Quality Data Related to Exceptional Events

State and local agencies and EPA are in the process of reviewing ozone data for purposes of making decisions regarding the exclusion of data under the Exceptional Events Rule. We will include these decisions regarding specific data that should be excluded from consideration when determining the amount of rollback of air quality to meet the current or alternative ozone standards.

2.3 Development of Estimates of Ozone Air Quality Assuming "Just Meeting" Current NAAQS and Potential Alternative NAAQS

2.3.1 Background and Conceptual Overview

In order to simulate air quality concentrations that "just meet" the current or potential alternative ozone standards in a study area, we consider what mathematical approach (commonly referred to as rollback) should be used to transform recent air quality into profiles of adjusted air quality that simulate just meeting the current or alternative standards under consideration.

The challenge in developing estimates of ozone air quality for a scenario in which an assessment location is "just meeting" the current standards or alternative standards under consideration is to estimate as realistically as possible how concentrations for all hours at all monitors will be affected, not just how the design value from the controlling monitor (or set of monitors being averaged) will be affected. The definition of "just meeting" alternative ozone standards uses the same approach as "just meeting" the current standards.

There are many possible ways to create characterizations of air quality to represent scenarios "just meeting" specified ozone standards. The previous two reviews have used a method called quadratic rollback, which is described below in section 2.3.2. This choice was based on analyses of historical ozone data which found, from comparing the reductions over time in daily ambient ozone levels in two locations with sufficient ambient air quality data, that

reductions tended to be roughly quadratic (Abt Associates, 2005, Appendix B). We recognize that the pattern of changes that have occurred in the past may not necessarily reflect the temporal and spatial patterns of changes that would likely result from future efforts to attain the ozone standards; therefore, we are considering examining an alternative prospective approach for rollback, as described in section 2.3.3.

2.3.2 Historical Approach

Prior ozone risk assessments simulated ozone reductions that would result from just meeting a set of standards using a quadratic adjustment ("quadratic rollback") which decreased non-background ozone levels on all hours for all concentrations exceeding the policy-relevant background (PRB). The portion of the distribution below the estimated PRB concentration was not rolled back, since air quality strategies adopted to meet the standards would not be expected to reduce the PRB contribution to ozone concentrations. The percentage amount of rollback was just enough so that the standard under consideration was not exceeded.

In the risk assessment for this review, we will again evaluate the quadratic rollback approach by comparing it with historical changes in distributions of ozone concentrations in selected locations. Specifically, EPA plans to evaluate historical ozone air quality changes to assess the implications of using a quadratic rollback approach. We also plan to consider the premises and outcomes of the quadratic rollback approach against our insights regarding known and likely future emission reductions, e.g., whether it is reasonable to expect that future patterns of changes in ozone air quality would generally be similar to historical patterns of changes in air quality.

2.4 Policy Relevant Background

A key issue to be addressed in the ozone Policy Assessment is the characterization of policy-relevant background ozone levels in the U.S. Historically, PRB has been defined as the distribution of ozone concentrations that would be observed in the U.S. in the absence of anthropogenic (man-made) emissions of ozone precursors in the U.S., Canada, and Mexico. This definition allows for analyses that focus on the effects and risks associated with pollutant levels

that have the potential to be controlled by U.S. regulations, through international agreements with border countries, or by voluntary emissions reductions in the U.S. and elsewhere.

For this assessment, we are planning to estimate concentrations for different background scenarios using the global-scale chemistry-transport model GEOS-Chem (Bey et al., 2001) to inform a discussion of how to characterize PRB. The GEOS-Chem model is run on a global scale and will be used to provide estimates of transported pollutants from emissions of natural and anthropogenic sources from various geographic areas. The details of this modeling approach are briefly summarized below.

The GEOS-Chem modeling system will be run using emissions and meteorological data for three annual periods (2006, 2007, 2008). EPA staff is considering how to best use these model results in the exposure and risk analyses, which will be based on 2008 – 2010 air quality. The GEOS-Chem model will be run using two nested grids. The outer grid will be global in extent and utilize a grid resolution of 2.0 by 2.5 degrees. The inner grid will be centered over North America, cover the area from 140-40W / 10-70N, and use a horizontal resolution of 0.50 by 0.67 degrees. Four scenarios will be modeled. First, a current atmosphere (base case) simulation will be completed using all global anthropogenic and natural emissions sources. A model performance evaluation will be completed for this scenario using surface air quality measurements and satellite estimates of atmospheric air pollutant concentrations.

In addition to the "current atmosphere" or base case run which includes all anthropogenic and biogenic emissions, GEOS-Chem will be run for three additional emissions scenarios to isolate the contributions of internationally transported air pollutants to ozone concentrations in the U.S.:

- A simulation in which U.S. anthropogenic emissions of nitrogen oxides (NO_X), non-methane volatile organic compounds (nMVOC), and carbon monoxide (CO) are set to zero, while anthropogenic emissions outside of the U.S. are maintained at their current levels.
- A simulation in which U.S., Canada, and Mexico anthropogenic emissions of NO_X, nMVOC, and CO are set to zero, while anthropogenic emissions outside of these areas are maintained at their current levels. This was referred to as policy relevant background (PRB) in the previous review of the ozone NAAQS.

- A simulation in which global anthropogenic emissions of NO_X, nMVOC, and CO are set to zero.

These simulations will allow us to quantify the contribution of U.S. anthropogenic, Canada and Mexico anthropogenic, international (excluding Canada and Mexico) anthropogenic, and natural ozone sources to U.S. ozone health risk individually. Since emissions of methane are at current levels for all of these simulations, we will consider differentiating the contribution of global methane emissions from natural sources using recently published modeling studies that examine the effect of perturbations in the methane mixing ratio on global and U.S. air quality (Fiore et al., 2008, 2009).

A growing body of observational and modeling studies suggests that the international anthropogenic contribution to U.S. background ozone levels is substantial and is expected to rise in the future as rapid economic development continues around the world. Of particular concern is rising Asian emissions of nitrogen oxides (NOx), which can influence U.S. ozone concentrations in the near-term, and methane, which affects background ozone concentrations globally over decadal time scales. The model simulations of current anthropogenic emissions described above will not allow for projections of future ozone background concentrations nor the contribution from specific global methane sources on ozone in the present. However, a large multi-model ensemble assessment convened by the Task Force on Hemispheric Transport of Air Pollution (TF HTAP) has produced estimates that may be informative for estimating future global background concentrations and concentrations transported from upwind regions. In particular, the HTAP 2010 Assessment Report[1] estimated that the contribution of NOx, non-methane VOC, and CO emissions in Europe, South Asia, and East Asia to North American ozone concentrations at relatively unpolluted sites is 32% of the contribution of emissions from all four regions (including North America) combined. That contribution is projected to rise to 49% in a conservative emissions growth scenario and to 52% in a scenario of aggressive global economic development. The report also concluded that approximately 40% of the mean global ozone increase since the preindustrial era is due to methane, and that rising global methane emissions will have a large influence on future U.S. ozone concentrations. These results may be

[1] Available at http://www.htap.org/

used to inform estimates of growth of international transport in the future and how those changes might affect our estimation of future ozone health risks.

2.5 Broader Air Quality Characterization

Information presented in the REA will draw upon air quality data analyzed in the ISA as well as national and regional trends in air quality as evaluated in EPA's Air Quality Status and Trends document (U.S. EPA, 2008a), and EPA's Report on the Environment (U.S. EPA, 2008b). We plan to use this information, and additional analyses, as needed, to develop a broad characterization of current air quality across the nation. For example, tables of areas and population in the U.S. exceeding current ozone standards and potential alternative standards will be prepared. Additional information will be generated on the expected number of days on which the ozone standards are exceeded, adjusting for the number of days monitored. Further, ozone levels in locations and time periods relevant to areas assessed in key short-term epidemiological studies discussed further in Section 5.3.2 will be characterized. Information on the spatial and temporal characterization of ozone across the national monitoring network will be compiled. To the extent possible, we plan to compare these data to the same parameters in the selected urban study areas considered in the quantitative risk assessment to help place the results of that assessment into a broader context.

3 APPROACH FOR POPULATION EXPOSURE ANALYSIS

3.1 Introduction

Population exposure to ambient ozone levels will be evaluated using the current version of the Air Pollutants Exposure (APEX) model, a model based on the current state of knowledge of inhalation exposure modeling. Exposure estimates will be developed for current ozone levels, based on 2008-2010 air quality data, and for ozone levels associated with just meeting the current 8-hour ozone NAAQS and alternative ozone standards, based on adjusting 2008-2010 air quality data. Exposure estimates will be modeled for 3 to 12 urban areas located throughout the U.S. for 1) the general population, 2) school-age children (ages 5 to 18), 3) asthmatic school-age children, 4) outdoor workers, and 5) the elderly population (aged 70 and older). This choice of population groups includes a strong emphasis on children, which reflects the results of the last review in which children, especially those who are active outdoors, were identified as the most important at-risk group.

The exposure estimates will be used as an input to that part of the health risk assessment that is based on exposure-response relationships derived from controlled human exposure studies, discussed in Section 4.3 below. The exposure analysis will also provide information on population exposure exceeding levels of concern that are identified based on evaluation of health effects that are not included in the quantitative risk assessment. It will also provide a characterization of populations with high exposures in terms of exposure environments and activities.

3.2 The APEX Population Exposure Model

APEX, also referred to as the Total Risk Integrated Methodology/Exposure (TRIM.Expo) model (U.S. EPA, 2008c,d), has its origins in the NAAQS Exposure Model (NEM), which was developed in the early 1980's (Biller et al., 1981; McCurdy, 1994, 1995). APEX simulates the movement of individuals through time and space and their exposure to a given pollutant in indoor, outdoor, and in-vehicle microenvironments. Figure 3-1 provides a schematic overview of the APEX model. The model stochastically generates simulated individuals using census-derived probability distributions for demographic characteristics (Figure 3-1, steps 1-3). The

population demographics are from the 2000 Census data at the tract or block level, and a national commuting database based on 2000 Census data provides home-to-work commuting flows between tracts. A large number of simulated individuals are modeled, and collectively, they represent a random sample of the study area population.

Diary-derived time activity data are used to construct a sequence of activity events for each simulated individual consistent with the individual's demographic characteristics and accounting for effects of day type (e.g., weekday, weekend) and outdoor temperature on daily activities (Figure 3-1, step 4). APEX calculates the concentration in the microenvironment associated with each event in an individual's activity pattern and sums the event-specific exposures within each hour to obtain a continuous time series of hourly exposures spanning the time period of interest (Figure 3-1, steps 5 and 6). From these exposure estimates, APEX calculates exposures for averaging times greater than one hour.

Figure 3-1. Overview of the APEX Model

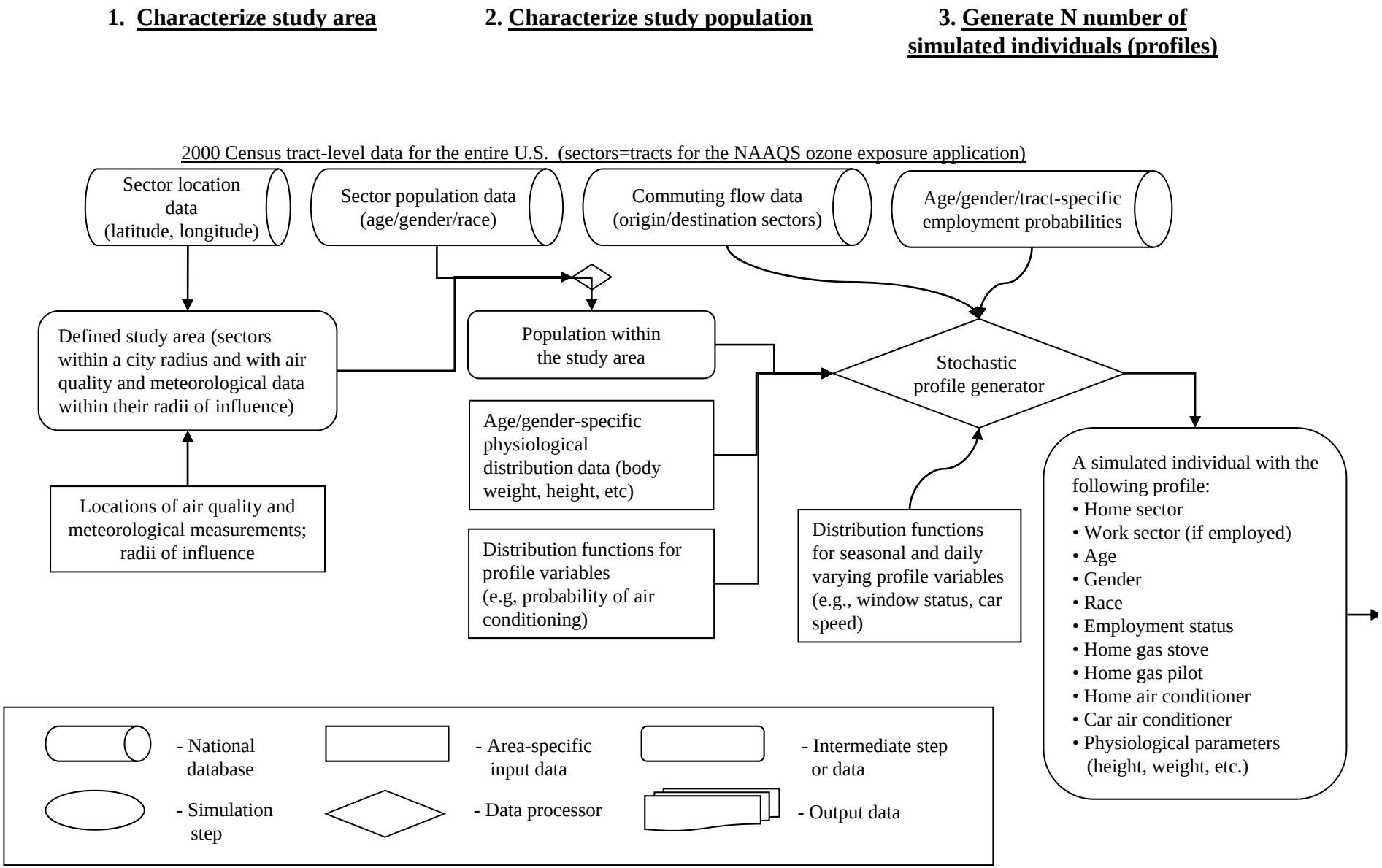


Figure 3-1. Overview of the APEX Model, continued

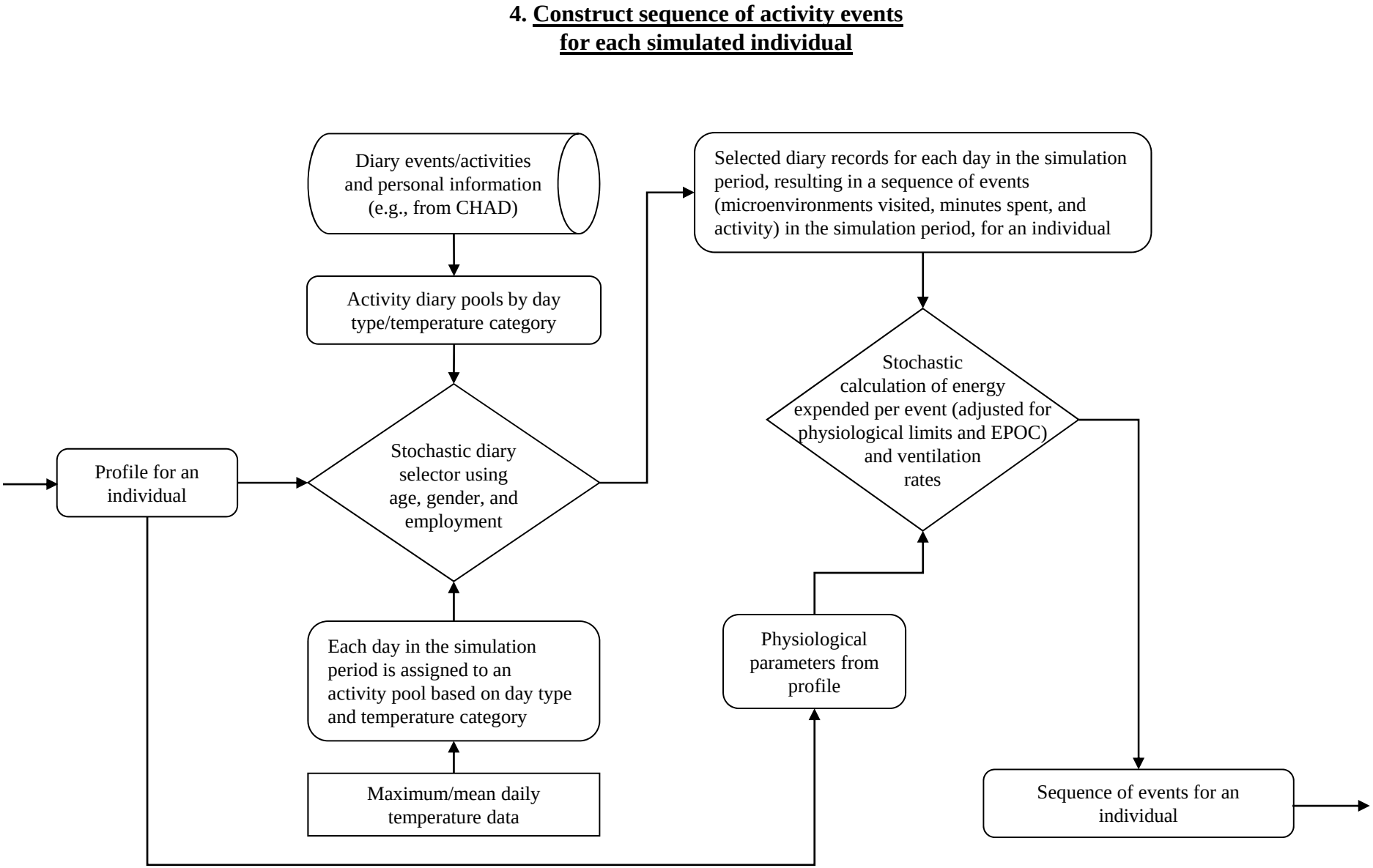
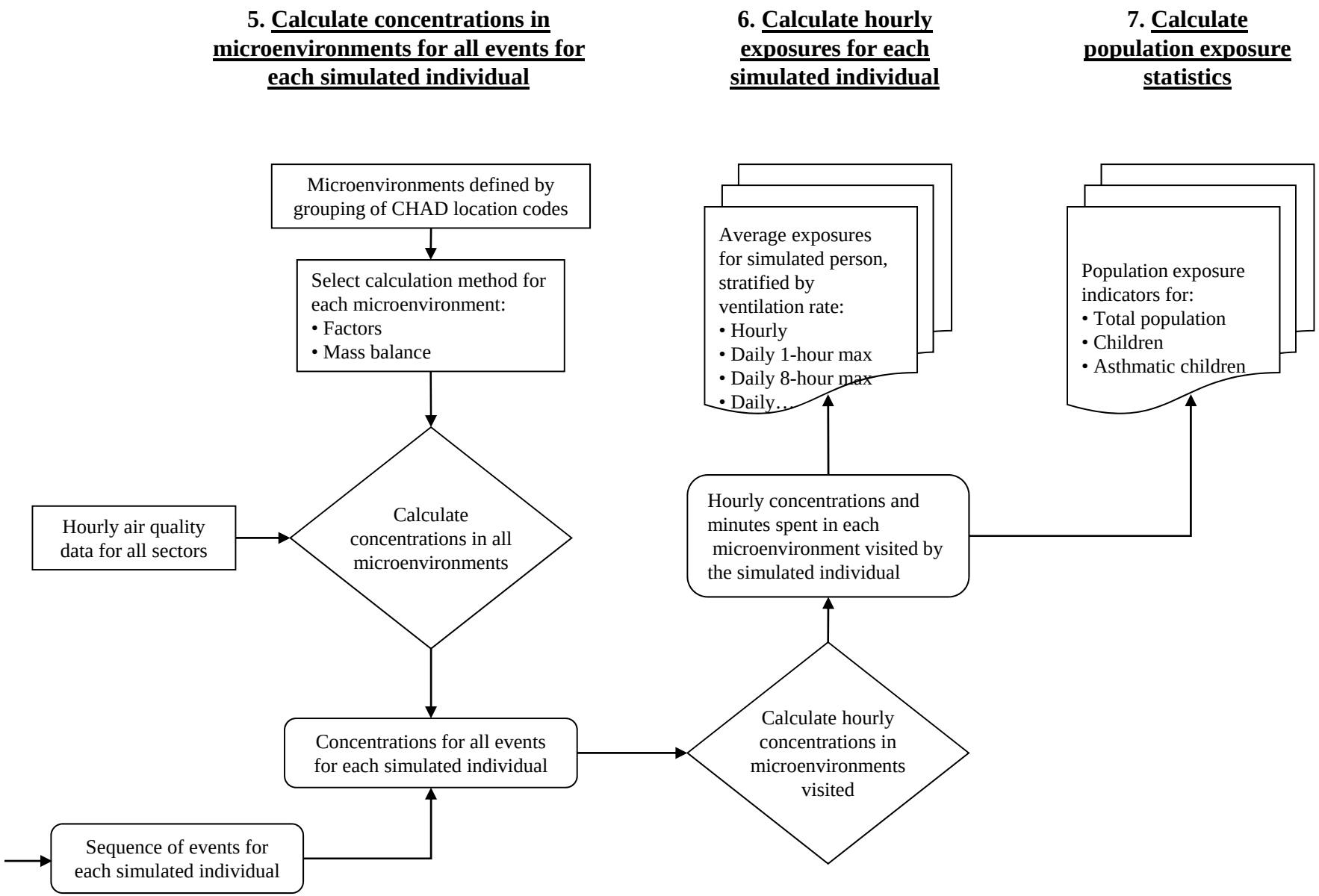


Figure 3-1. Overview of the APEX Model, concluded



APEX employs a flexible approach for simulating microenvironmental concentrations, where the user can define any number of microenvironments to be modeled and their characteristics. For this modeling application, we propose modeling the microenvironments listed in Table 3-1.

Table 3-1. Microenvironments to be Modeled

Microenvironment	Method
Indoors – residences	mass balance
Indoors – restaurants	mass balance
Indoors – schools	mass balance
Indoors – offices	mass balance
Indoors – shopping	mass balance or factors
Indoors – other	mass balance or factors
Outdoors – public garages and parking lots	factors
Outdoors – near road (walking, bicycling)	factors
Outdoors – other (e.g., playgrounds, parks)	factors
In vehicle – cars and light trucks	mass balance or factors
In vehicle – heavy trucks	mass balance or factors
In vehicle – school buses	mass balance or factors
In vehicle – mass transit vehicles – buses and trolleys	factors
In vehicle – mass transit vehicles – underground (subways)	factors

We plan to calculate the concentrations in each microenvironment using either a factors or mass-balance approach[1], depending upon data availability, with probability distributions representing variability of the parameters that enter into the calculations (e.g., indoor-outdoor air exchange rates) supplied as inputs to the model. These distributions represent the variability (not uncertainty) of parameters, and can vary spatially and can be set up to depend on the values of other variables in the model. For example, the distribution of air exchange rates in a home,

[1] The factors and mass-balance approaches are described in section 3.6.5.

office, or car depends on the ambient temperature and the type of heating and air conditioning present. The value of a stochastic parameter can be kept constant for an individual for the entire simulation (e.g., house volume), or a new value can be drawn hourly, daily, or seasonally from specified distributions. APEX also allows the specification of diurnal, weekly, and seasonal patterns for microenvironmental parameters.

3.3 Populations Modeled

A detailed consideration of the population residing in each modeled area will be included. The exposure assessment will include the general population residing in each area modeled as well as susceptible and vulnerable populations as identified in the ISA. The population groups that we plan to include in the exposure assessment are:

- The general population
- School-age children (ages 5 to 18)
- Asthmatic school-age children
- Outdoor workers
- The elderly population (aged 70 and older)

Due to the increased amount of time spent outdoors engaged in relatively high levels of physical activity, school-age children as a group are particularly at risk for experiencing ozone-related health effects as a result of to their increased dose rates. The proportion of the population of school-age children characterized as being asthmatic will be estimated by statistics on asthma prevalence rates from the National Health Interview Survey (CDC, 2010) and other sources.

3.4 Outcomes to be Generated

There are several useful indicators of exposure of people to various levels of air pollution. Factors that are important in defining such indicators include the magnitude and duration of exposures, frequency of repeated high exposures, and ventilation rate (i.e., breathing rate) of the individual at the time of exposure. In this analysis, exposure indicators will include daily maximum 1- and 8-hour average ozone exposures, stratified by equivalent ventilation rates (i.e., ventilation normalized by body surface area).

APEX calculates two general types of exposure estimates: counts of people and person-occurrences. The former counts the number of individuals exposed one or more times per ozone

season to the exposure indicator (e.g., exposure level and ventilation rate) of interest. In the case where the exposure indicator is a benchmark concentration level, 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 measure counts the number of times per ozone season that an individual is exposed to the exposure indicator of interest and then accumulates counts over all individuals. Therefore, the person-occurrences measure conflates people and occurrences: using this measure, 1 occurrence for 10 people is counted the same as 10 occurrences for 1 person.

Analyses of the APEX results will provide distributions of the numbers of people with 8-hour average exposure above benchmark levels of 0.06, 0.07, and 0.08 ppm-8 hours, distributions of the numbers of people with lung function decrements above 10, 15, and 20 percent decreases in FEV_1, and characterization of the attributes of highly exposed individuals.

3.5 Selection of Urban Areas and Time Periods

EPA plans to model population exposures to ambient ozone in three or more of the 12 urban areas modeled in the previous review (Atlanta, Boston, Chicago, Cleveland, Detroit, Houston, Los Angeles, New York City, Philadelphia, Sacramento, Seattle, St. Louis, Washington, D.C.) and a high-altitude city, such as Denver. These were selected to be generally representative of a variety of populations, geographic areas, climates, and different ozone and co-pollutant levels, and are areas where epidemiologic studies have been conducted that are planned to be used to support the quantitative risk assessment.

The exposure periods to be modeled will be the ozone-monitoring seasons for each urban area. These encompass the periods when high ambient ozone levels are likely to occur, and are the periods for which routine hourly ozone monitoring data are available. The ozone seasons for the selected study areas generally range from April through either September or October for most of the locations in the eastern U.S. to all year in locations in southern California and Texas.

3.6 Development of Model Inputs

In this section, we describe the plan for developing the inputs to the APEX model.

3.6.1 Population Demographics

We plan to use tract-level population counts from the 2000 Census of Population and Housing Summary File 1[1]. Summary File 1 (SF 1) contains the 100-percent data, which is the information compiled from the questions asked of all people and about every housing unit.

In the 2000 U.S. Census, estimates of employment were developed by census tract[2]. The file input to APEX will be broken down by gender and age group, so that each gender/age group combination is given an employment probability fraction (ranging from zero to 1) within each census tract. The age groupings in this file 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. Children under 16 years of age will be assumed to be not employed.

3.6.2 Commuting

As part of the population demographics inputs, it is important to integrate working patterns into the assessment. In addition to using estimates of employment by tract, APEX also incorporates home-to-work commuting data. We plan to use the national commuting database provided with APEX in this analysis. Commuting data were derived from the 2000 Census and were collected as part of the Census Transportation Planning Package (CTPP) (U.S. DOT, 2000)[3]. The data used to generate APEX inputs were taken 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 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.

3.6.3 Ambient Ozone Concentrations

We plan to conduct exposure modeling based on ozone concentrations measured at ambient air monitors in and near the areas being modeled. Sources for these data include the

[1] http://www.census.gov/prod/cen2000/doc/sf1.pdf
[2] Employment data from the 2000 Census can be found on the U.S. Census web site: http://www.census.gov/population/www/cen2000/phc-t28.html (Employment Status: 2000- Supplemental Tables).
[3] These data are available from the U.S. DOT Bureau of Transportation Statistics (BTS) at the web site: http://transtats.bts.gov/.

hourly concentration measurements from the monitoring data maintained in EPA's Air Quality System (AQS).

3.6.4 Meteorological Data

Surface meteorological observations will be obtained from the National Climatic Data Center[1] to provide hourly temperatures for input to APEX. We plan to use all meteorological stations within and nearby each selected urban study area.

3.6.5 Specification of Microenvironments

Parameters defining each microenvironment will be specified by distributions which reflect the variability of these parameters. The parameters needed depend on whether a microenvironment is modeled using the factors model or the mass balance model.

We plan to use the factors model to model simple environments, like outdoor areas, that do not contain pollutant sources, or microenvironments for which 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 concentration outside of the microenvironment ($\boldsymbol{C}_O$) 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 microenvironment from outside the microenvironment. The concentration inside the microenvironment ($\boldsymbol{C}_I$) is estimated by the equation $\boldsymbol{C}_I = \boldsymbol{F}_{inf}\,\boldsymbol{C}_O$. The infiltration factor in the factors 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 microenvironment-specific distributions specified by the user, to model the stochastic nature of these factors.

The mass balance model is more appropriate for complex environments. The mass balance method assumes that an enclosed microenvironment (e.g., a room in a residence) is a

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

single well-mixed volume in which the air concentration is approximately spatially uniform. APEX estimates the concentration of an air pollutant in such a microenvironment by using the following four processes (as illustrated in Figure 3-2):

- Inflow of air into the microenvironment;
- Outflow of air from the microenvironment;
- Removal of a pollutant from the microenvironment due to deposition, filtration, and chemical degradation; and
- Emissions from sources of a pollutant inside the microenvironment.

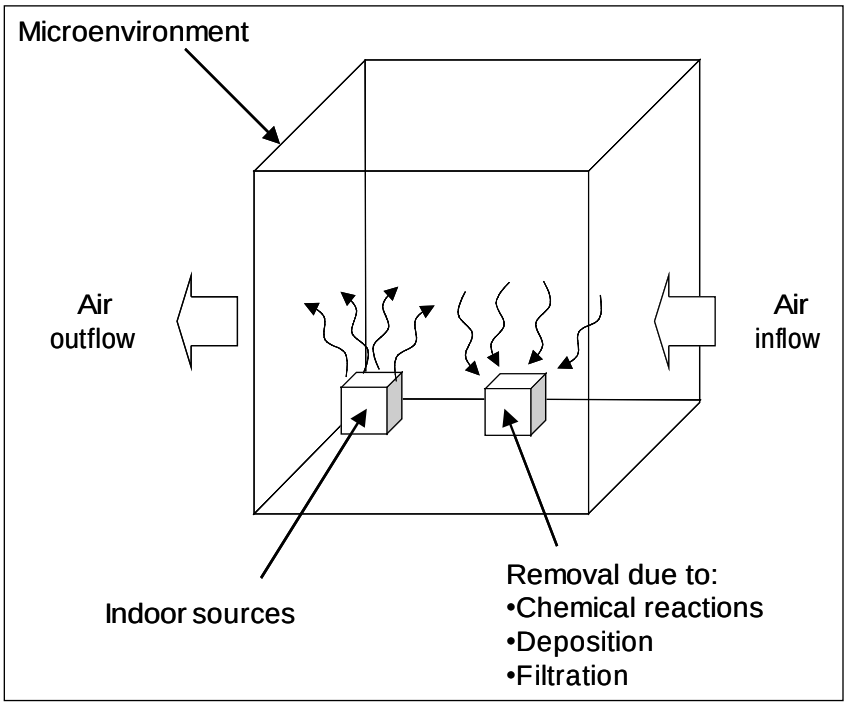


Figure 3-2. The Mass Balance Model

Considering the microenvironment as a distinct, well-mixed volume of air, the mass balance relationship for a pollutant can be described by:

$$\frac{dC(t)}{dt} = \frac{dC_{in}(t)}{dt} - \frac{dC_{out}(t)}{dt} - \frac{dC_{loss}(t)}{dt} + \frac{dC_{source}(t)}{dt}$$

where:

$C(t)$ = Concentration in the microenvironment at time t (µg/m^3)

$\frac{dC_{in}(t)}{dt}$ = Rate of change in C(t) due to air entering the micro

$$\frac{dC_{out}(t)}{dt} = \text{Rate of change in C(t) due to air leaving the micro}$$

$$\frac{dC_{loss}(t)}{dt} = \text{Rate of change in C(t) due to all removal processes}$$

$$\frac{dC_{source}(t)}{dt} = \text{Rate of change in C(t) due to all source terms}$$

In addition to proximity factors, this method 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 microenvironment-specific parameters based on available data and a review of the literature.

3.6.6 Indoor Sources

We are considering modeling indoor sources of ozone in this analysis, although our focus is on exposure to ozone of ambient origin. Indoor sources of ozone would not be subject to "rollback."

3.6.7 Activity Patterns

Exposure models use human activity pattern data to predict and estimate exposure to pollutants. Different human activities, such as outdoor exercise, indoor reading, or driving, have different pollutant exposure characteristics. In addition, different human activities require different metabolic rates, and higher rates lead to higher doses. To accurately model individuals and their exposure to pollutants, it is critical to have a firm understanding of their daily activities.

The Consolidated Human Activity Database (CHAD) provides data on human activities through a database system of collected human diaries, or daily activity logs (McCurdy et al., 2000; U.S. EPA, 2002; Graham and McCurdy, 2004). The purpose of CHAD is to provide a basis for conducting multi-route, multi-media exposure assessments (McCurdy et al., 2000). The data contained within CHAD come from multiple surveys with varied structures (Table 3-2). In general, the surveys have a data foundation based on daily diaries of human activity. Individuals filled out diaries of their daily activities and this information was entered and stored in CHAD. Relevant data for these individuals, such as age, are included as well. In addition, CHAD contains activity-specific metabolic distributions developed from literature-derived data, which are used to provide an estimate of metabolic rates of respondents through their various activities.

The locations used in the CHAD diaries must be assigned appropriately to the APEX microenvironments listed in Table 3-1. Each of the microenvironments is designed to simulate an environment in which people spend time during the day. There are many more CHAD locations than microenvironments being modeled (there are over 100 CHAD locations and 14 proposed microenvironments modeled in this assessment) thus, most of the microenvironments have multiple CHAD locations mapped to them.

Table 3-2. Studies In CHAD To Be Used For Exposure Modeling

Study name	Geographic coverage	Study time period	Subject ages	Diary−days	Number of subjects	Diary type and study design	Reference
Baltimore	One building in Baltimore	1/1997−2/1997, 7/1998−8/1998	72 − 93	391	26	Diary	Williams et al. (2000)
California Adults (CARB)	California	10/1987−9/1988	18 − 94	1,552	1,552	Recall (next day telephone survey); Random	Robinson et al. (1989), Wiley et al. (1991a)
California Children (CARB)	California	04/1989−2/1990	<1 − 11	1,200	1,200	Recall (next day telephone survey); Random	Wiley et al. (1991b)
California Adolescents (CARB)	California	10/1987−9/1988	12 − 17	181	181	Recall (next day telephone survey); Random	Robinson et al. (1989), Wiley et al. (1991a)
Cincinnati (EPRI)	Cincinnati metro. area	3/1985, 8/1985	<1 − 86	2,601	884	Diary; Random	Johnson (1989)
Denver (EPA)	Denver metro. area	11/1982−2/1983	18 − 70	798	438	Diary; Random	Johnson (1984), Akland et al. (1985)
Los Angeles: Elementary School	Los Angeles	10/1989	10 − 12	49	17	Diary	Spier et al. (1992)
Los Angeles: High School	Los Angeles	10/1990	13 − 17	42	19	Diary	Spier et al. (1992)
NHAPS[2]−Air	National	9/1992−9/1994	<1 − 93	4,338	4,338	Recall; Random	Klepeis et al. (1996), Tsang and Klepeis (1996)
NHAPS−Water	National	9/1992−9/1994	<1 − 93	4,349	4,349	Recall; Random	Klepeis et al. (1996), Tsang and Klepeis (1996)

Study name	Geographic coverage	Study time period	Subject ages	Diary−days	Number of subjects	Diary type and study design	Reference
PSID CDS[3] I	National	3/1997−6/1997, 9/1997−12/1997	<1 − 13	4,989	2,706	Diary; Random	Hofferth et al. (1999)
PSID CDS II	National	10/2002−6/2003	5 − 19	4,774	2,505	Diary; Random	Mainieri et al. (2004)
Seattle	Seattle, WA	12/2000−5/2001	6 − 91	1,688	178	Diary	Liu et al. (2003)
RTI Ozone Averting Behavior	National	7/2002–9/2002	2 – 12	2,882	773	Recall; Random	Mansfield and Corey (2003), Mansfield et al. (2004; 2006)
RTP Panel	Chapel Hill, Raleigh, NC	6/2000−5/2001	55 − 85	1,000	37	Diary	Williams et al. (2003a,b)
RTI NSAS	8 cities[4]	6/2009–9/2009	35-92	4,383	1,194	Recall; Random	Knowledge Networks (2009)
Washington, D.C.	Wash., D.C. metro. area	11/1982−2/1983	18 − 98	699	699	Diary; Random	Hartwell et al. (1984), Akland et al. (1985)
Totals				**35,916**	**21,096**		

NOTE: The counts in this table refer to subsets of the studies in CHAD for which data are suitable for use in APEX.

[2] National Human Activity Pattern Survey. http://www.exposurescience.org/NHAPS

[3] The Panel Study of Income Dynamics, Child Development Supplement. http://psidonline.isr.umich.edu/

[4] Atlanta, Chicago, Dallas, Houston, Philadelphia, Sacramento/San Joaquin, St. Louis, Washington D.C.

3.7 Exposure Modeling Issues

In this section, we highlight some aspects of the proposed exposure modeling that have the potential to significantly contribute to uncertainties in the exposure analysis. These aspects of people's exposures are either not modeled or are based on limited information.

- **Representativeness of Personal Activity Patterns**

The human activity data will be drawn from the CHAD developed and maintained by the Office of Research and Development's (ORD) National Exposure Research Laboratory (NERL). The CHAD includes data from several surveys covering specific time periods at city, state, and national levels, with varying degrees of representativeness. The extent to which the human activity database provides a balanced representation of the population being modeled varies across areas. Although the algorithm that constructs activity sequences attempts to account for the effects of population demographics and local climate on activity, this adjustment procedure does not fully account for all intercity differences in people's activities. Activity patterns are affected by many local factors, including topography, land use, traffic patterns, mass transit systems, and recreational opportunities. If time and resources permit, to improve the representativeness of the activity patterns, diaries from the American Time Use Survey (Bureau of Labor Statistics, 2010; Tudor-Locke et al., 2009, 2010) will be included in the activity pattern database used by APEX. The American Time Use Survey (ATUS) provides nationally representative estimates of how and where Americans spend their time. The ATUS data files include information collected from over 98,000 interviews conducted from 2003 to 2009. The current CHAD database has about 40,000 diaries that APEX can use (Table 3-2), so this has the potential to be a significant improvement. The ATUS data are collected through telephone interviews asking about the previous day's activities, and measure the amounts of time people that spend doing various activities, such as work, childcare, housework, watching television, exercising, and socializing.

- **Longitudinal Personal Activity Patterns**

In the previous review, it was found that APEX significantly underestimates the frequency of occurrence of individuals experiencing repeated 8-hour average exposures greater than 0.06, 0.07, and 0.08 ppm (Langstaff, 2007). The assignment of activity diaries to individuals is the primary determinant of the frequency of repeated exposures for individuals. This is an important consideration, since multiple exposures pose a greater health concern than single exposures. The current methodology for the construction of a year-long activity sequence for each individual does increase the

similarity of daily activities for a given simulated individual in terms of the time spent outdoors, compared to a random assignment of diaries from CHAD to modeled individuals (Glen et al., 2008). However, repeated routine behavior from one weekday to the next is not simulated. For example, there are no simulated individuals representing children in summer camps who spend a large portion of their time outdoors, or adults with repeating weekday schedules. Improvement of the current approach for creating year-long activity sequences will be undertaken if sufficient resources are available. We believe an appropriate approach should adequately account for the day-to-day and week-to-week repetition of activities common to individuals while maintaining realistic variability between individuals.

- **Averting Behavior**

Behavior changes in response to ozone pollution or in response to air quality index (AQI) notification ("averting behavior") can affect the population distribution of exposures, and was not modeled in the previous review. Eiswerth et al. (2005) find that increased ozone levels appear to influence the amount of time that asthmatic adults spend in different activities. In a national survey, Mansfield and Corey (2003) find a significant fraction of the people surveyed modifying their activities in response to ozone alerts. Significant research on averting behavior has been conducted since the last review (Di Novi, 2010; Neidell, 2010, 2005a, 2005b; Neidell et al., 2010; Semenza, 2008; Wen et al., 2009). A methodology for accounting for averting behavior will be developed for this assessment if sufficient resources are available.

- **Modeling Near-Traffic Outdoor Environments and Public Transportation**

Modeling activities such as walking next to roads, waiting at bus stops, bicycling, and riding motorcycles, buses, subways and trains is difficult due to the limited information available about these activities. It is also difficult to estimate the ambient concentrations in these environments. Ozone concentrations in these environments are typically lower than measurements at centrally located monitors as a result of the titration of ozone by the NO emissions of the vehicles. A number of near-road monitoring studies have been conducted since the last review. An analysis of monitoring data to improve estimates of exposures near-roadways will be undertaken if sufficient resources are available.

- **Metabolic equivalent (MET) distributions for activities**

The distributions of activity-specific MET values are of fundamental importance to the physiological model in APEX and therefore to the estimates of lung function decrements. Johnson (2003, section 9.6) states:

> Perhaps the weakest link in the algorithm is the step which requires the analyst to provide a distribution of possible MET values for each activity code. These distributions are currently based on distributions provided by the developers of CHAD (McCurdy et al., 2000). Because available data were often insufficient to accurately define a distribution for each activity code, the developers tended to follow a conservative approach and over-estimate the variability of each distribution. Consequently, the Ve values produced by the ventilation rate algorithm may exhibit an excessive degree of variability.

McCurdy et al. (2000), in a paper describing the development of the MET distributions in CHAD, state:

> At this stage of development, the METs distribution assignment effort should be viewed as being preliminary in nature. More work is needed to better relate activity codes used in human activity pattern surveys to those long used by exercise physiologists and clinical nutritionists.

Staff will review the recent literature related to MET distributions and update the distributions used by APEX, if sufficient resources are available.

3.8 Uncertainty and Variability

The primary difficulty in performing an exposure modeling uncertainty analysis is the quantitative characterization of the uncertainties of the model inputs and model formulation. Information about the variability of model inputs or the variability and uncertainty combined is often available, but it is usually difficult to estimate the uncertainty separately from the variability. In considering the use of APEX for an ozone exposure assessment, EPA has considered the availability of information to provide plausible distributions or ranges for the uncertainties of all of the model inputs. EPA plans to build upon the APEX exposure modeling uncertainty analysis conducted in support of the previous review of the ozone NAAQS (Langstaff, 2007). We plan to improve on these distributions of variability and uncertainty, where data are available to do so, and to extend the analysis of model formulation uncertainty.

Once estimates of the uncertainty of the model inputs have been developed, we plan to propagate these uncertainties through the model to quantify the resultant uncertainty of the model predictions. The APEX uncertainty analysis methodology incorporates a 2-dimensional Monte Carlo sampling approach that explicitly characterizes and models the variability and uncertainty in inputs and outputs. Essentially, this approach entails performing thousands of

model runs with model inputs randomly sampled from specified distributions reflecting uncertainty of the model inputs, while each single APEX run simulates distributions of variability. This 2-dimensional Monte Carlo method allows for the separate characterization of the variability and uncertainty in the model results (Morgan and Henrion, 1990; Cullen and Frey, 1999). This approach allows for great flexibility in specifying uncertainty distributions for any of the model inputs and parameters that are supplied to APEX by input files. Furthermore, this allows us to specify conditional distributions and joint distributions between parameters for which we have data, which can be critically important in modeling uncertainty (Haas, 1997; Haas, 1999; Wu and Tsang, 2004).

Uncertainties are inherent in modeled representations of physical reality due to simplifying assumptions and other aspects of model formulation. The methods for assessing input parameter uncertainty and model formulation or structure uncertainty are different. It is difficult to incorporate the uncertainties due to the model formulation into a quantitative assessment of uncertainty in a straightforward manner. The preferred way to assess model formulation uncertainty is by comparing model predictions with measured values, while having fairly complete knowledge of the uncertainty due to input parameters. EPA plans to ascertain whether sufficient data are available to perform such an evaluation. For example, we will consider using the data collected in the Detroit Study (DEARS[1]) for this purpose. In the absence of measurements that can be used to estimate model uncertainty, our planned approach to assessing model formulation uncertainty will be to partition this uncertainty into that of the components, or sub-models, of APEX. For each of the sub-models within APEX, we plan to discuss the simplifying assumptions and those uncertainties associated with the sub-models which are distinct from the input data uncertainties. Where possible, we plan to evaluate these sub-models by comparing their predictions with measured data. Alternatively, we may formulate an informed judgment as to a range of plausible uncertainties for the sub-models. We plan to quantitatively assemble the different types of uncertainties and variability to present an integrated analysis of uncertainty and variability.

[1] See http://www.epa.gov/dears

4 ASSESSMENT OF HEALTH RISK BASED ON CONTROLLED HUMAN EXPOSURE STUDIES

4.1 Introduction

The major components of the portion of the health risk assessment based on data from controlled human exposure studies are illustrated in Figure 2. The air quality and exposure analysis components that are integral to this portion of the risk assessment are discussed above in Sections 2 and 3, respectively. As described in the draft ozone ISA (U.S. EPA, 2011b) and previous ozone Criteria Documents (U.S. EPA, 1996b, 2006), there are numerous controlled human exposure studies reporting lung function decrements (as measured by changes in FEV_1), as well as changes in other measures of lung function, airway responsiveness, respiratory symptoms, and various markers of inflammation. Most of these studies have involved voluntary exposures with healthy adults, although a few studies have been conducted with mild and moderate asthmatics and one study reported lung function decrements for children 8-11 years old (McDonnell et al., 1985).

Staff plans to develop lung function decrement risk estimates for the general population, school age children, asthmatic school age children, outdoor workers, and the elderly population (aged 70 and older) living in 12 urban areas in the U.S. These areas, identified previously in Section 3.2, represent a range of geographic areas, population demographics, and ozone climatology. As discussed further in Section 4.4.2, the selection of these areas was also influenced by whether other health endpoints could be examined in the same urban area based on concentration-response relationships developed from epidemiological or field studies.

4.2 Selection of Health Endpoints

In the last review, the health risk assessment estimated lung function decrements (≥ 10, ≥ 15, and $\geq 20\%$ changes in FEV_1) in children 5-18 years old associated with 8-hour exposures at moderate exertion. At that time EPA staff and the CASAC Ozone Panel judged that it was reasonable to estimate the exposure-response relationships for children 5-18 years old based on data from adult subjects (18-35 years old). As discussed in the 1996 Ozone Staff Paper (EPA, 1996a) and 1996 ozone Criteria Document (EPA, 1996b), findings from other chamber studies (McDonnell et al., 1985) for children 8-11 years old and summer camp field studies in at least

six different locations in the United States and Canada found lung function changes in healthy children similar to those observed in healthy adults exposed to ozone under controlled chamber conditions. Staff intends to use the same approach in this assessment.

4.3 Selection of Exposure-Response Functions

The health risk assessment conducted in this new review will build on the approach developed and applied in the 2008 rulemaking. In that previous assessment, risk estimates for lung function responses associated with 8-hour exposures while engaged in moderate exertion were developed. These estimates were based in part on exposure-response relationships estimated from the combined data sets from multiple ozone controlled human exposure studies. Data from the studies by Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991) in addition to more recent data from Adams (2002, 2003, 2006) were used to estimate exposure-response relationships for $\geq$ 10, 15, and 20% decrements in FEV_1.

The data from these controlled human exposure studies are 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 of ozone during the course of an exposure. Generally, this correction for exercise in clean air is small relative to the total effects measures in the ozone-exposed cases. Regression techniques are then used to fit a function to the data. A Bayesian approach is used then to characterize uncertainty attributable to sampling error based on sample size considerations. Response rates are calculated for 21 fractiles (for cumulative probabilities from 0.05 to 0.95 in steps of 0.05, plus probabilities of 0.01 and 0.99) at a number of ozone concentrations (see U.S. EPA, 2007a for details of this approach).

4.4 Approach to Calculating Risk Estimates

Staff plans to generate several risk measures for this portion of the risk assessment. In addition to the estimates of the number of school age children and other groups experiencing one or more occurrences of a lung function decrement $\geq$ 10, $\geq$ 15, and $\geq$ 20% in an ozone season, risk estimates also will be developed for the total number of occurrences of these lung function decrements in school age children and active school age children.

A headcount risk estimate for a given lung function decrement (e.g., ≥ 20% change in FEV_1) is an estimate of the expected number of people who will experience that lung function decrement. Since EPA is interested in risk estimates associated with ozone concentrations in excess of policy relevant background concentrations, staff plans to (1) estimate expected risk, given the personal exposures associated with ambient ozone concentrations, (2) estimate expected risk, given the personal exposures associated with estimated background ambient ozone concentrations, and (3) subtract the latter from the former. As shown in equation 4-1 below, the headcount risk is then calculated by multiplying the resulting expected risk by the number of people in the relevant population. Because response rates are calculated for 21 fractiles, estimated headcount risks are similarly fractile-specific.

The risk (i.e., expected fractional response rate) for the k^{th} fractile, R_k is:

$$R_k = \sum_{j=1}^{N} P_j \; x \; (RR_k \mid e_j) \quad - \quad \sum_{i=1}^{N_b} P_i^b \; x \; (RR_k \mid e_i^b) \qquad (4\text{-}1)$$

where:

e_j = (the midpoint of) the jth category of personal exposure to ozone, under "as is" ambient ozone concentrations;

e_i^b = (the midpoint of) the ith category of personal exposure to ozone, under background ambient ozone concentrations;

P_j = the fraction of the population having personal exposures to ozone concentration of e_j ppm, under "as is" ambient ozone concentrations;

P_i^b = the fraction of the population having personal exposures to ozone concentration of e_i^b ppm, under background ambient ozone concentrations;

$RR_k \mid e_j$ = k-fractile response rate at ozone concentration e_j;

$RR_k \mid e_i^b$ = k-fractile response rate at ozone concentration e_i^b; and

N = number of intervals (categories) of ozone personal exposure concentration, under "as is" ambient ozone concentrations; and

N_b = number of intervals of ozone personal exposure concentration, under background ambient ozone concentrations.

For example, if the median expected response rate under "as is" ambient concentrations is 0.065 (i.e., the median expected fraction of the population responding is 6.5%) and the median expected response rate under background ambient concentrations is 0.001 (i.e., the median

expected fraction of the population responding is 0.1%), then the median expected response rate associated with "as is" ambient concentrations above policy relevant background concentrations is 0.065 – 0.001 = 0.064. If there are 300,000 people in the relevant population, then the headcount risk is 0.064 x 300,000 = 19,200.

4.5 Alternative Approach Under Consideration For Calculating Risk Estimates

In this new review, if adequate resources are available, staff intends to investigate the possibility of using an improved model that estimates FEV_1 responses for individuals associated with short-term exposures to ozone (McDonnell, Stewart, and Smith, 2010). This model is based on the controlled human exposure data included in the prior lung function risk assessment as well as additional data sets for different averaging times and breathing rates. These data were from 15 controlled human ozone exposure studies that included exposure of 541 volunteers (ages 18–35 years) on a total of 864 occasions (see McDonnell et al., 2007, for a description of these data).

This model calculates the FEV_1 decrement due to ozone exposure for each diary event as:

$$\%\Delta FEV1_{ijk} = e^{Ui}\left\{\frac{\beta_1+\beta_2 y_{ijk}}{1+\beta_4\, e^{-\beta_3 Xijk}} - \frac{\beta_1+\beta_2 y_{ijk}}{1+\beta_4}\right\} \quad (4\text{-}2)$$

where X is given by the solution of the differential equation (4-3):

$$\frac{dX}{dt} = C(t)V(t)^{\beta_6} - \beta_5 X(t) \quad (4\text{-}3)$$

In APEX, because the exposure concentration, exertion level, and ventilation rate are constant over an event, this equation has an analytic solution for each event (events range in duration from 1 to 60 minutes):

$$X(t) = X(t_o)\, e^{-\beta_5(t-t0)} + \frac{C(t)}{\beta_5} V(t)^{\beta_6}(1 - e^{-\beta_5(t-t0)}) \quad (4\text{-}4)$$

where

$C(t)$ is the exposure concentration at time t (ppm),
$V(t) = VE(t)/BSA$ is the effective ventilation rate at time t (L min^{-2} m^{-2}),
$VE(t)$ is the expired minute volume at time t (L min^{-2}),
BSA is the body surface area (m^2),
X_0 is the value of X(t) at time t_0,
t is the time (minutes), t_0 is the time at the start of the event,

$y_{ijk} = \alpha_1 Age + \alpha_2$, (age in years; α_1 and α_2 depend on age range) and
U_i = subject-level random effect (zero mean).

The *y* term is a function of the age of the individual in years. In the equation from McDonnell, Stewart, and Smith (2010), y is given as [Age_{ijk} – 25], however this term was developed using only data from individuals aged 18-35. Using a larger data set that included individuals with ages ranging from 8 to 76, we performed a piecewise linear fit of the form $y = \alpha_1 Age + \alpha_2$, for different ranges of ages. The three linear fits (ages 8-16, 16-35, 35-100) match at each boundary to form a continuous function of age. Exposure data used for the youth fit came from McDonnell et al. 1985, Avol et al. 1987, and Avol et al. 1985. Exposure data for the 36-76 age range were taken from Drechsler-Parks et al. 1987, Drechsler-Parks et al. 1989, Gong et al. 1997, and Hazucha et al. 2003.

For youth, we found $\%\Delta FEV_1$ to be highly correlated with age, with a linear regression giving: $y = -3.16 Age + 41.58$; but for older adults, we found it only varied weakly with age: $y = 0.02 Age + 9.3$. The middle age range ($y = Age - 25$) of 18-35 was extended to younger ages, 16-35, based on discussions with McDonnell. No data exist for the range age < 8, and due to rapid changes in the physiology of children (as opposed to adults), extension of the fit to lower age ranges is increasingly uncertain and will not be done. Accordingly, $\%\Delta FEV_1$ will not be modeled for children under 8 years of age. The parameters α_1 and α_2 are age-dependent and are specified in the APEX physiology input file. Staff will conduct further analyses to inform the choice of these parameters.

Here, β_1 - β_6 and the variance of the $\{U_i\}$ are unitless fitted model parameters (see McDonnell, Stewart, and Smith (2010) for details of fit). Values of U are drawn from a Gaussian distribution with mean zero and variance var(U). They are chosen once for each individual and remain constant throughout the simulation. The best fit values for these parameters given by McDonnell, Stewart, and Smith (2010) are as follows (to 3 significant figures) : $\beta_1 = 9.90$, $\beta_2 = -0.411$, $\beta_3 = 0.0164$, $\beta_4 = 46.9$, $\beta_5 = 0.00375$, $\beta_6 = 0.912$, Var(U) = 0.835.

Staff intends to perform an evaluation of this model based on data from clinical studies that were not used in the development of the model.

4.6 Uncertainty and Variability

Staff plans to conduct a 2-dimensional Monte Carlo analysis of the uncertainty and variability of the risk estimates based on data from controlled human exposure studies. This will of necessity be integrated with the exposure modeling uncertainty assessment.

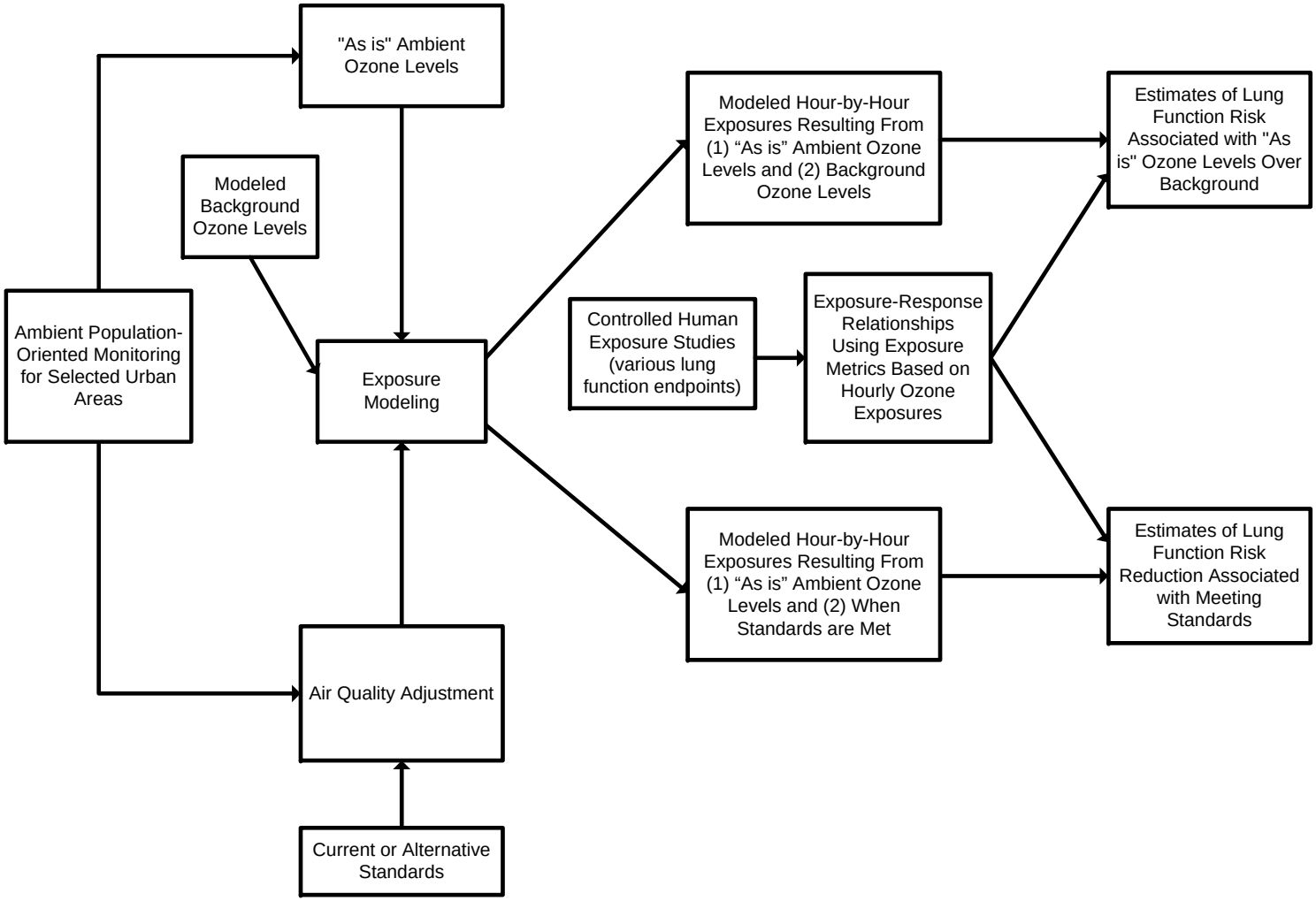


Figure 4-1. Major Components of Ozone Health Risk Assessment Based on Controlled Human Exposure Studies

5 ASSESSMENT OF HEALTH RISK BASED ON EPIDEMIOLOGIC STUDIES

5.1 Introduction

As discussed in the draft ozone ISA (EPA, 2011b), a significant number of epidemiological and field studies examining a variety of health effects associated with ambient ozone concentrations in various locations throughout the U.S., Canada, Europe, and other regions of the world have been published since the last NAAQS review. As a result of the availability of these epidemiological and field studies and air quality information, staff plans to expand the ozone risk assessment to include an assessment of selected health risks attributable to ambient ozone concentrations over policy relevant background concentration and health risk reductions associated with attainment of current and alternative ozone standards in selected urban locations in the U.S. The major components of the portion of the health risk assessment based on data from epidemiological and field studies are illustrated in Figure 5-1. The approaches used by staff to select health endpoint categories, urban areas, and epidemiology and field studies to consider for inclusion in the risk assessment are discussed below.

This chapter presents an overview of the design of the human health risk assessment to be conducted in the current review of the ozone NAAQS. This design reflects goals laid out in the Integrated Review Plan (U.S. EPA, 2011a, section 5.5) including: (1) to provide estimates of the potential magnitude of premature mortality and/or selected morbidity health effects in the population associated with recent ambient ozone levels and with just meeting the current suite of ozone standards and any alternative standards that might be considered in selected urban study areas; (2) to develop a better understanding of the influence of various inputs and assumptions on the risk estimates; and (3) to gain insights into the distribution of risks and patterns of risk reduction and uncertainties in those risk estimates.

Based upon the information assessed in the first draft ISA, we plan to focus the risk assessment on health effect endpoints for which the weight of the evidence as assessed in the ISA supports the judgment that the overall health effect category is at least likely caused by exposure to ozone either alone and/or in combination with other pollutants. The planned quantitative risk assessment, is designed to estimate risks associated with short-term (≥ 24-hour

average) and long-term (e.g., annual- or seasonal- average) ambient ozone concentrations in selected urban study areas. We are considering expanding the focus of this risk assessment to include additional health effect categories beyond those classified as casual or likely causal, when available evidence presented in the ISA is sufficiently suggestive of a causal association to support conducting quantitative risk assessment and when inclusion of that endpoint category will allow us to address potentially important policy issues related to reviewing the ozone NAAQS. For example, we are considering including information on birth outcome effects associated with ambient ozone which would allow us to evaluate additional potentially sensitive populations (i.e., pregnant women and infants) not previously evaluated in the quantitative risk assessment conducted in the last review. In addition, we are also considering estimating respiratory mortality associated with long-term exposure to ozone.[1] EPA recognizes that a decision to include these additional endpoint categories needs to consider the increased uncertainty that their inclusion could introduce into the risk assessment; specifically, the potential for these endpoints not to be causally linked with ozone exposure, despite the statistical associations observed in epidemiological studies.

Building upon the assessment completed in the last review, we plan to focus the ozone assessment on modeling risk for a set of selected urban study areas, chosen in order to provide population coverage and to portray the observed heterogeneity in ozone-related risk across selected urban study areas. EPA is considering ways to put the quantitative risk assessment results conducted for a limited number of locations and selected health endpoints into a broader context to better characterize the nature, magnitude, extent, variability, and uncertainty of the public health impacts associated with ozone exposures.

In designing the risk assessment, we expect to identify multiple options for specifying specific elements of the risk model (e.g., several concentration response functions for a particular health endpoint; several approaches for characterizing ambient ozone levels within urban areas using monitors and/or modeling data). In these instances, to the extent possible given available information, we will identify those options that we believe has the greatest support in the

[1] As noted in section 5.1, the decision to model long-term exposure-related respiratory mortality is complicated by the fact that, while the draft ISA classifies all-cause mortality related to long-term ozone exposure has having a suggestive of a casual association, the draft ISA assigns respiratory morbidity as likely to have a causal association.

literature. These modeling elements will then be used, to generate a core (base case) set of risk estimates. The remaining options identified for specifying elements of the risk model will be used as part of the sensitivity analysis (see below) to generate an additional set of reasonable risk estimates that can be used to provide a context, with regard to uncertainty, within which to assess the set of core (base case) risk results. Note, that in general, those health effects endpoints falling within health effects endpoint categories assigned a causal or likely causal association with ozone exposure will be included in the core analysis, while endpoints assigned a suggestive of a causal association (if modeled quantitatively) would likely be included as part of the sensitivity analysis. As noted earlier, respiratory mortality associated with long-term exposure represents a special case. Depending on how we ultimately interpret the degree of support for an association with this endpoint and ozone exposure, we may include this endpoint as part of the core estimate, or retain it as a component of the sensitivity analysis.

As part of the risk assessment, we will address both uncertainty and variability. In the case of uncertainty, we are planning to use a four-tiered approach developed by the World Health Organization (WHO) and used in the risk assessment completed for the last PM NAAQS review. The WHO's four-tiered approach matches the sophistication of the assessment of uncertainty to the overall complexity of the risk assessment, while also considering the potential magnitude of the impact that the risk assessment can have from a regulatory/policy perspective (e.g., risk assessments that are complex and are associated with significant regulatory initiatives would likely be subjected to more sophisticated uncertainty analysis). The WHO framework includes the use of sensitivity analysis both to characterize the potential impact of sources of uncertainty on core risk estimates and (as noted earlier) to generate an alternative set of reasonable risk estimates that supplement the core risk estimates.

In the case of variability, we will identify key sources of variability associated with ozone risk (for both short-term and long-term exposure-related endpoints included in the risk assessment) and discuss the degree to which these sources of variability are reflected in the design of the risk assessment. Note, that in those cases where a particular source of variability is not sufficiently reflected in core risk estimates, this can introduce uncertainty and potentially bias into the risk estimates since representativeness can be reduced (in certain cases, the sensitivity

analysis may also explore these sources of variability given their potential to introduce uncertainty into core risk estimates).

As part of the analysis, we will also complete a representativeness analysis designed to support the interpretation of risk estimates generated for the set of urban study areas included in the risk assessment. The representativeness analysis will focus on comparing the urban study areas to national-scale distributions for key ozone-risk related attributes (e.g., demographics including socioeconomic status, air-conditions use, baseline incidence rates and ambient ozone levels). The goal with these comparisons will be to assess the degree to which the urban study areas provide coverage for different regions of the country as well as for areas likely to experience elevated ozone-related risk due to their specific mix of attributes related to ozone risk. As part of the representativeness analysis, we are also considering a broader national-scale assessment of mortality (both short- and long-term exposure-related). These national-scale mortality estimates would also allow us to assess the degree to which the urban study areas included in the risk assessment provide coverage for areas of the country expected to experience elevated mortality rates due to ozone-exposure. We note that a national-scale assessment such as this was completed for the risk assessment supporting the latest PM NAAQS review (U.S. EPA, 2010) with the results of the analysis being used to support an assessment of the representativeness of the urban study areas (assessed in the PM NAAQS risk assessment), as described here for ozone. Additional detail on the representativeness analysis is presented in section 5.4.5.

The following discussion begins by presenting the framework for the risk assessment developed to evaluate ozone with more detailed discussions of key components of the risk assessment model including air quality considerations (section 5.2). Next, we discuss the selection of health effects endpoints to include in the assessment, including the specification of concentration-response (C-R) functions, baseline incidence data and demographic data (section 5.3). We conclude with the discussion of how uncertainty and variability will be addressed in the analysis (section 5.4). This discussion also includes an overview of the representativeness analysis planned for the assessment.

5.2 Framework for the Ozone Health Risk Assessment

5.2.1 Overview of Modeling Approach

Consistent with the last review, we plan to quantify the number of ozone-related adverse health outcomes by using a health impact function, the components of which are illustrated in equation 5-1. The health impact function combines information about changes in ambient ozone air quality concentrations (Δx) with C-R relationships (reflected by β, the ozone coefficient derived from epidemiological studies) and baseline health incidence data for specific health endpoints (y) to derive estimates of the change in incidence (Δy) of specific health effects attributable to ambient ozone concentrations during the period examined among a particular population (*Pop*).[1]

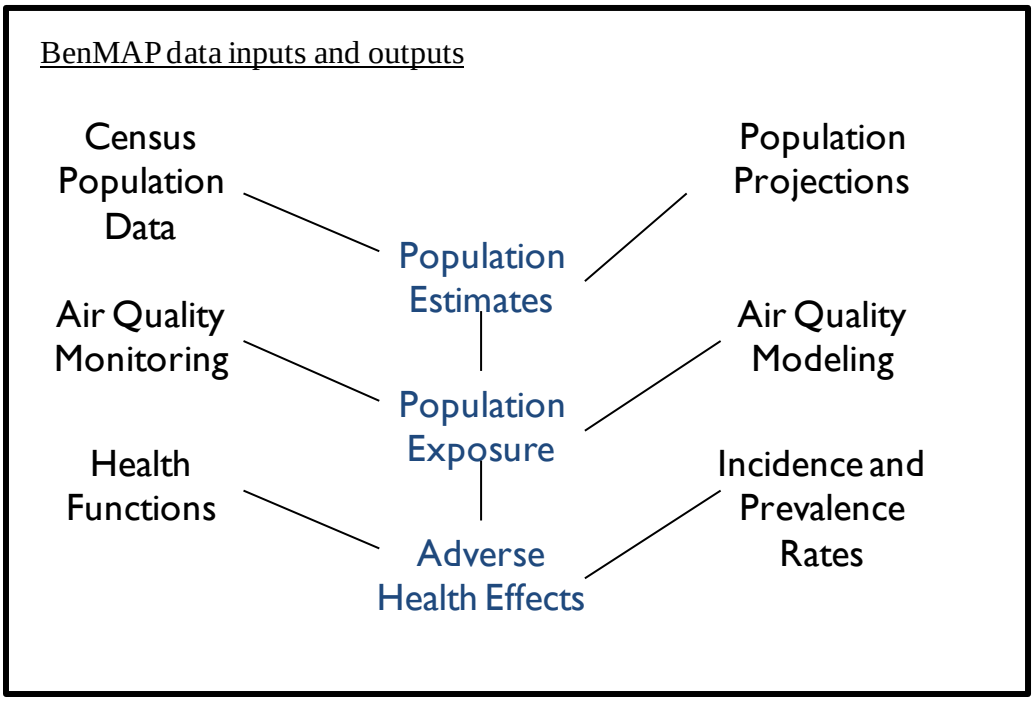
$$\Delta y = y\ e^{\beta \Delta x} - 1\ Pop \qquad (5\text{-}1)$$

This type of risk model applies risk coefficients drawn from epidemiological studies that characterize the relationship between ambient ozone levels measured at fixed-site population-oriented monitors and the risk of specific health endpoints in the population. Therefore, it does not require more detailed individual-level exposure modeling described above and relies instead on the use of ambient monitoring data. Specifically, a change in the level of ambient ozone is translated through the risk coefficient (β) to a change in the baseline rate of a particular health effect(s) in the study population. This adjustment to the baseline incidence rate can then be combined with population estimates (*Pop*) to generate a change in the incidence of a specific health endpoint(s) attributable to a change in ambient ozone.

In this review we plan to use the environmental Benefits Mapping and Analysis Program (BenMAP) (Abt, 2008) to perform this calculation across multiple health impact functions and urban areas. This GIS-based computer program draws upon a database of population, baseline incidence and effect coefficients to automate the calculation of health impacts. EPA has traditionally relied upon the BenMAP program to estimate the health impacts avoided and economic benefits associated with adopting new air quality rules. For this analysis, EPA will use

[1] The health risk model given in Equation 5-1 is based on a concentration-response function in which the natural logarithm of the incidence of the health effect is a linear function of ozone concentration. We plan to consider other mathematical forms where epidemiological studies have reported effects using other model forms.

the model to estimate ozone-related impacts among the health endpoints, and within the urban areas, discussed below. BenMAP already contains much of the population and baseline incidence data, and many of the effect coefficients, needed to perform this analysis; where it does not, we will specify the model with the appropriate data. The following diagram summarizes the data inputs (in black text) and outputs (in blue text) for a typical BenMAP analysis.



BenMAP offers several advantages in terms of modeling population exposure and risk. First, once we have properly specified the BenMAP software, the program can produce risk estimates for an array of modeling scenarios across a large number of urban areas. Second, the program can accommodate a variety of sensitivity analyses. For example, we may consider the sensitivity of our risk estimates to alternative specifications of concentration-response functions for the same endpoint. Third, BenMAP would be useful to performing a national assessment of ozone mortality for the purposes of a representativeness analysis (as discussed earlier in section 5.1).

As described in Figure 5-1, this risk assessment approach requires specifying a number of modeling components related to (a) characterizing air quality, (b) establishing the C-R functions,

and (c) specifying the baseline incidence rates and population demographics. The remainder of this section discusses each of these modeling components in detail.

5.2.2 Air Quality Considerations

There are several air quality inputs to the risk assessment as illustrated in Figure 5-1. These have been described in Chapter 2 and include: (a) characterization of recent air quality (i.e., ambient ozone levels) for each selected urban study area, (b) background concentrations for each selected urban study area, and (c) projections of ambient air quality for both current and alternative ozone NAAQS under consideration. Additional detail on these inputs is presented below:

- **Characterizing recent ambient ozone levels for selected urban study areas using monitoring data:** EPA plans to use 3 years (2008-2010) of ambient ozone measurement data to characterize recent air quality conditions (see section 2.2). In aggregating monitoring data (to form composite monitor(s) for each study area) and linking those monitors to study populations within a particular study area, as noted earlier in section 2.2, we are considering two approaches. As in the previous ozone NAAQS risk assessment, we plan to match, to the extent possible, the approach for analyzing air quality data used in the epidemiological studies from which the C-R functions are obtained. For example, in order to be consistent with the approach generally used in the epidemiological studies from which C-R functions have been estimated for effects associated with long-term ozone exposures, we plan to develop and use ambient data for a single composite monitor based on monitored data from all eligible monitors in that study area. Some epidemiological studies have used more sophisticated (and spatially-refined) methods for associating ambient ozone data with a study population. In cases where we include C-R functions from studies using alternative methods to link ambient ozone concentrations with health effects information in our risk assessment, we may consider a more refined approach for linking ozone monitoring data with study populations, to match the approach used in the study. However, in addition to a risk simulation where we attempt to match our use of monitoring data to the approach used in the underlying epidemiological studies, we are also considering an alternative approach where we focus on developing composite monitors that are more representative of exposure profiles experienced by populations currently. As noted in section 2.2, this could involve an alternative weighting scheme for deriving composite monitors where we use the results of micro-environmental exposure modeling (used in the

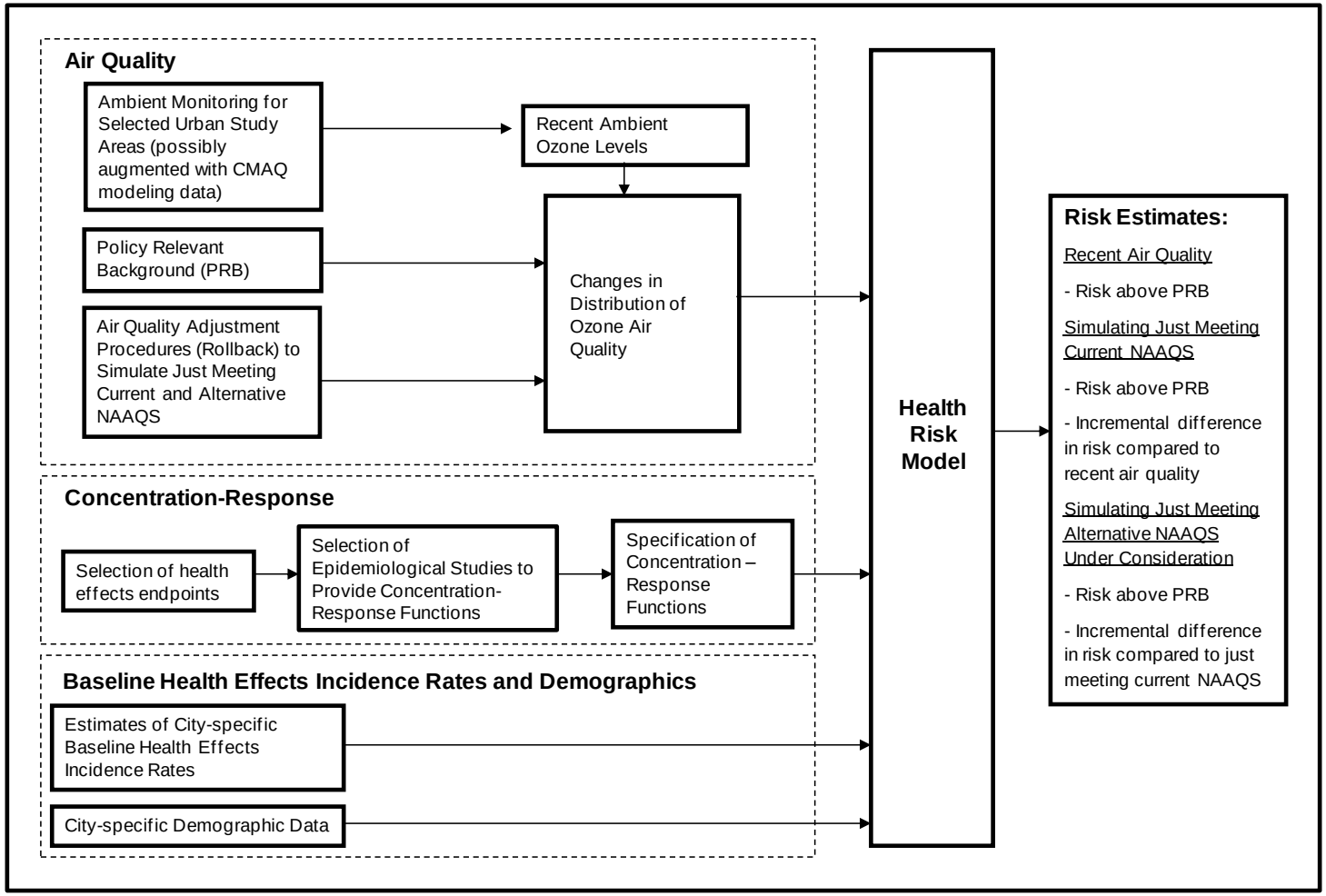


Figure 5-1. Overview of Risk Assessment Model Based on Epidemiologic Studies

exposure analysis – see Section 3) to generate weights for each monitor in an urban study area reflecting the fraction of population exposure associated with that monitor (e.g., the fraction of simulated person-ozone hours associated with the area surrounding a given monitor). The details of this approach are still being developed.

- **Characterizing recent ambient ozone levels for selected urban study areas using a combination of monitoring and modeled data:** As discussed in section 2.2, we are also considering the use of monitor data augmented with modeling in characterizing recent ambient ozone conditions. This type of a fused surface has the benefit of retaining the ambient characterization of absolute ozone levels (at monitors), while using modeled concentrations to characterize the spatial gradient between monitors. Note, however, that we would still need to specify how this more spatially-refined surface would be related to population in order to generate an exposure surrogate (e.g., would we conduct risk simulation at a more spatially-refined grid cell-level, or would we use the more differentiated ozone surface to generate a composite measurement value – a single value for the entire study area)? The decision as to whether to pursue this type of fused (model-monitor) surface and if so, how to use it in characterizing exposure, would likely rely heavily on our assessment of the spatial heterogeneity of ozone levels across a subset of our urban study areas – see bullet below.

- **Assessment of spatial heterogeneity of ozone across urban study areas:** As noted in section 2.2., a potentially important component of designing the risk assessment involves an assessment of the spatial heterogeneity of ambient ozone levels across prospective urban study areas. This assessment would likely be based on consideration for the pattern of ozone levels (daily time series and seasonal/annual averages) across monitors within a given urban study area. If spatial heterogeneity across monitors is found to be low (and more specifically, if temporal profiles for the monitors within a given study area are similar), then there may be little benefit in using more sophisticated approaches for linking ambient ozone levels and populations within a given study area. Conversely, if there is substantial spatial heterogeneity, then the representativeness of an exposure surrogate (e.g., surrogate monitor) could be enhanced by more closely linking ambient ozone levels to demographics.

- **Characterizing PRB**: As noted in section 2.4, we will rely on characterization of PRB provided by GEOS-Chem modeling to obtain values specific to each urban study area included in the risk assessment. However, we will likely consider several different background definitions (e.g., U.S. background, a North American background, and natural background).

- **Method for adjusting ambient air quality levels to simulate air quality just meeting current and potential alternative ozone NAAQS**: As discussed in section 2.3, EPA is planning to use the quadratic rollback approach to simulate ozone levels to just meet current and alternative NAAQS standards. Note, that we may explore the degree of spatial heterogeneity associated with ambient ozone levels within our urban study areas. If we find that there is substantial spatial heterogeneity, then this could mean that the pattern of rollback potentially associated with attainment of an alternative (lower) level could be more complex from a spatial standpoint (i.e., there is potentially, increased uncertainty in simulating attainment of either the current or alternative standards). Conversely, if we find that there is limited spatial heterogeneity, then we expect that uncertainty associated with simulating alternative standard levels would be relatively lower.

5.3 Selection of Health Effects Endpoint Categories

As noted in section 5.1, based on review of the first draft ISA, we plan to focus the risk assessment on ozone, estimating potential health impacts associated with both short-term and long-term exposures to ozone. In selecting health effects endpoints to include in the risk assessment, we have considered the following factors based upon review of the first draft ISA (U.S. EPA, 2011b; Chapters 2, 6, and 7): (a) the extent to which the health effect endpoints are considered significant from a public health standpoint, (b) the overall weight of the evidence from the collective body of epidemiological, clinical, and toxicological studies and the inferences made in the first draft ISA as to whether there is a causal or likely causal relationship between ozone and the health effect endpoint category, (c) whether there is sufficient evidence to support a causal or likely causal relationship for the specific health endpoint within the health effect category to warrant inclusion in the risk assessment, and (d) whether there are well-conducted studies reporting estimated C-R functions for specific health endpoints associated with ambient ozone levels.

Based upon review of the first draft ISA, we plan to consider the following health effect endpoint categories in this assessment:

Health Effect Categories Associated with Short-term Ozone Exposure

- respiratory morbidity (causal association)
- mortality (likely causal association)

Health Effect Categories Associated with Long-term Ozone Exposure

- respiratory morbidity (likely casual association)

In addition to the health effect categories presented above, we are considering expanding the focus of the ozone risk assessment to include additional endpoints from health effect categories that have been initially judged in the first draft ozone ISA to have a suggestive causal association with ambient ozone measurements. We plan to consider including these additional endpoints when they allow us to address potentially important policy issues related to reviewing the current ozone standards. Risk estimates for endpoints within these additional health effects categories would likely not be presented as part of the core risk assessment, but rather would be included as part of the sensitivity analysis examining additional potential health effects endpoints. Potential health effect endpoint categories being considered for inclusion in the sensitivity analysis include: (a) long-term exposure-related birth outcome effects (allows us to evaluate potentially sensitive populations, including pregnant women and infants), and (b) long-term exposure-related respiratory mortality (due to the clear public health significance of this endpoint).

The respiratory mortality endpoint deserves some additional discussion. While the general all-cause mortality category was given a suggestive of causal association (for long-term exposure) in the draft ISA, it is important to note that the respiratory morbidity category (again for long-term exposure) was assigned a likely causal association classification in the draft ISA. If we consider focusing an assessment of long-term exposure related mortality on respiratory mortality (which would be the endpoint most supported by the latest reanalysis of the ACS data), then the appropriate causality association classification for this specific mortality endpoint may be more complicated to determine. While this endpoint falls within a category of mortality (which was assigned a suggestive of casual association), it is also a type of respiratory health effect (which is given a likely casual association). Therefore, EPA will continue to review information presented in the next draft ISA and look to input provided by both the public and CASAC to make a determination as to the appropriate degree of support to assign to the long-term exposure-related respiratory mortality category. Ultimately, this determination will result in

an estimate of respiratory mortality (if it is indeed generated in the first place) to be included as part of the core estimate, or retained as part of the sensitivity analysis.

5.3.1 Selection of Epidemiological Studies and Specification of Concentration-Response Functions

As noted above, the risk assessment conducted in this review will build on the approach developed and applied in the last review. EPA will rely on a weight-of evidence approach, based on the ISA's evaluation of new and previously reviewed epidemiologic studies including identification of relevant C-R functions that characterize the relationships between short- and long-term ozone exposures and health outcomes, particularly those conducted at or near current ambient concentrations. Quantitative relationships provided in the specific studies (or to be derived by EPA from the data presented in the epidemiologic studies) describe the change in concentration (generally based on ambient fixed-site monitors) associated with a change in health response. These C-R relationships will be combined with air quality data, baseline incidence data, and population data to develop population health risk estimates.

We plan to use specific criteria to select the epidemiological studies that will be used to provide C-R functions for the quantitative risk assessment including:

- The study addresses one of the health effects endpoint categories identified for inclusion in the risk assessment.

- The study was peer-reviewed, evaluated in the first draft ISA, and judged adequate by EPA staff for purposes of inclusion in the risk assessment. Criteria considered by staff include: whether the study provides C-R relationships for locations in the U.S., whether the study has sufficient sample size to provide effect estimates with a sufficient degree of precision and power, whether the study is a multi-city study, and whether adequate information is provided to characterize statistical uncertainty.

- The study is not superseded by another study (e.g., if a later study is an extension or replication of a former study, the later study would effectively replace the former study), unless the earlier study has characteristics that are clearly preferable.

In addition to the above criteria, other factors, which may be specific to a particular health effect endpoint, or even to a set of studies, may be considered. For example, several of the studies have improved upon the method of estimating the exposure metric used in most studies which have generally relied upon population-oriented monitoring data. Instead of

assigning the same ambient ozone concentration to all individuals in a city (based on a central monitor or the average of several monitors in a city), these studies have assigned "exposures" according to monitors that better approximate conditions near subjects' residences. These and similar studies may provide additional insights into whether reductions in mortality are attributable to recent, or more historical changes in patterns of long-term ozone exposure.

We also plan to consider the overall study design, including the method used to adjust for covariates (including confounders and effects modifiers) in identifying candidate studies. For example, if a given study uses ecological-defined variables (e.g., smoking rates) as the basis for controlling for confounding, concerns may be raised as to the effectiveness of that control. These factors related to confounding control and consideration of effects modification also will be considered in identifying studies for use as the basis of C-R functions.

Once the final set of epidemiological studies is chosen, the next step will be the selection of C-R functions from those studies. A number of factors need to be considered in specifying C-R functions related to short- and long-term exposure studies. The factors being considered in selecting C-R functions include:

- **Single- and multi-pollutant models (*pertains to both short-term and long-term exposure studies*)**: Epidemiological studies often consider health effects associated with ambient ozone independently as well as together with co-pollutants (e.g., PM, nitrogen dioxide, sulfur dioxide, carbon monoxide). To the extent that any of the co-pollutants present in the ambient air may have contributed to health effects attributed to ozone in single pollutant models, risks attributed to ozone may be overestimated if C-R functions are based on single pollutant models. This would argue for inclusion of models reflecting consideration of co-pollutants. Conversely, in those instances where co-pollutants are highly correlated with ozone, inclusion of those pollutants in the health impact model can produce unstable and statistically insignificant effect estimates for both ozone and the co-pollutants. This situation would argue for inclusion of a model based exclusively on ozone. Given that single and multi-pollutant models each have potential advantages and disadvantages, we plan to include both types of C-R functions in the risk assessment.

- **Single-city versus multi-city studies (*typically a factor in short-term exposure studies)***: All else being equal, we judge C-R functions estimated in the assessment location as preferable to a function estimated in some other location, to avoid uncertainties that may

exist due to differences associated with geographic location. There are several advantages, however, to using estimates from multi-city studies versus studies carried out in single cities. Multi-city studies are applicable to a variety of settings, since they estimate a central tendency across multiple locations. Multi-city studies also tend to have more statistical power and provide effect estimates with relatively greater precision than single-city studies due to larger sample sizes, reducing the uncertainty around the estimated health coefficient. By contrast, single-city studies, while often having lower statistical power and varying study designs which can make comparison across cities challenging, do reflect location-specific factors such as differences in underlying health status, and differences in exposure-related factors such as air conditioner use and urban density with larger populations exposed near high-traffic roads. Because single- and multi-city studies have different advantages, we plan to include both types of functions in this analysis, where they are available. We plan to place greater weight on the use of C-R relationships reflecting adjusted single-city estimates from multi-city studies. This would include empirical Bayes adjusted city-specific estimates. These types of effect estimates benefit both from increased statistical power, as well as the potential for specification of city-specific effect estimates. Conversely, if a multi-city study only provides aggregated effect estimates, but does differentiate those estimates regionally, we plan to use those regional-specific estimates rather than a single national-level estimate by matching selected urban study areas to these regions.

- **Multiple lag models (*pertinent to short-term exposure time-series studies*)**: If information is available for a distributed lag model, we plan to use that model. Where there are multiple lags presented, but a distributed lag model is not included, we plan to consider information presented in the first draft ISA to determine if there is biological support for selecting a specific lag period for a given health effect endpoint.

- **Interactions between pollutants and temperature**: To the extent that studies explore (a) interactions between pollutant(s) and ozone and (b) interactions between temperature and ozone, we will consider that information in modeling specific endpoints to the extent that relevant concentration-response functions (taking into consideration these factors are available) and/or use this information to help interpreting risk estimates.

- **Seasonally-differentiated effects estimates (*pertinent to short-term studies*)**: In those instances where studies presented effect estimates associated with short-term ambient ozone concentrations differentiated by season, we plan to use these seasonal estimates. We plan to link seasonal effect estimates with seasonal ozone air quality data in conducting the risk assessment for selected urban study areas.

- **Shape of the functional form of the risk model:** In the risk assessment conducted in the last review, EPA included C-R relationships that reflected linear or log-linear C-R functions that extended down to estimated background levels for effects related to short-term exposure and down to lowest measured ambient levels for effects related to long-term exposure, as well as adjusting these models to reflect various alternative "cutpoint" models. The alternative cutpoint models imposed an assumed threshold on the original C-R function, below which there is little or no population response. The first draft ISA concludes that there is little support in the literature for a population threshold for short-term exposure-related effects, although in the case of mortality, the first draft ISA notes that the nature of the mortality effect as well as study design may mean that these studies are not well suited to identify a threshold should it exist (see U.S. EPA, 2011b, section 2.5.3.2). In the case of long-term exposure related endpoints (specifically for birth outcomes), the first draft ISA notes that study results suggest a clear association with ozone above approximately 30 ppb, with that relationship no longer being statistically significant below that level (i.e., a 95^{th}% confidence interval on the effect estimate including zero below this ambient ozone level). Given the above observation from the first draft ISA regarding the potential for thresholds, we are planning to (a) for all short-term exposure related endpoints, not consider a threshold either in the core analysis, or as part of sensitivity analyses and (b) for long-term exposure-related endpoints, consider a range of threshold levels (e.g., 20, 30 and 40 ppm) along with a no-threshold scenario. Note, that as discussed earlier, all simulations for birth outcomes (if conducted) will be presented as part of the sensitivity analysis. However, long-term exposure-related mortality (if run) could be included as part of the core risk estimate or as part of sensitivity analyses, depending on how we ultimately interpret the degree of support for a casual association. In either case, for long-term exposure-related mortality, we would also likely simulate a series of potential thresholds (e.g., 20, 30 and 40 ppb) with risk estimates for these simulations being included as part of the sensitivity analysis.

In addition to the factors listed above, there are additional factors related to the design of individual epidemiological studies which we plan to consider in selecting the C-R functions to be included in the assessment. For example, studies often include adjustment for covariates with varying degrees of freedom, reflecting the tradeoff between bias and over-adjustment (loss of efficiency). In these cases, we plan to consider any information provided for specific studies within the first draft ISA and also plan to consider which model form has the strongest statistical fit, while still considering overall biological plausibility. An additional factor that we will consider in selecting C-R functions to include in the risk assessment is ongoing research into the

potential mitigating and averting effect that air quality alerts such as the EPA's AirNOW can have on ozone-related exposure and risk. If available research is found to provide effect estimates (or information that can be used to derive effect estimates) that reflect this averting and/or mitigating activity by the exposed population, then we would consider including risks based on these adjusted effect estimates as part of our Sensitivity Analysis.

5.3.2 Selection of Urban Study Areas

We plan to build on the risk assessment conducted for the last review and continue to focus the risk assessment on a set of selected urban study areas. The decision to continue to focus on modeling a set of selected urban study areas reflects the goal of providing risk estimates that have higher overall confidence due to the use of location-specific data when available for these urban locations. In addition, given the greater availability of location-specific data, a more rigorous evaluation of the impact of uncertainty and variability can be conducted for a set of selected urban study areas than would be possible for a broader regional or national-scale analysis. We plan to consider the following factors in the selection of urban study areas:

- **Air quality data**: The urban area has sufficient recent (2008-2010) air quality data to conduct the risk assessment (See section 2.2.1).

- **Location-specific C-R functions**: There are C-R functions available from epidemiological studies that we ultimately select to use as the basis for deriving concentration-response functions, for one or more of the selected health endpoints. This primarily applies to short-term epidemiological studies, which more often include city-specific effect estimates. C-R functions available from long-term epidemiological studies generally combine data from multiple cities. Specific cities evaluated in the key long-term studies would be considered for inclusion in the risk assessment. We plan to include urban study areas that have been assessed in epidemiological studies that have evaluated health effects associated with both short- and long-term ozone exposures and, to the extent possible, locations where both morbidity and mortality health endpoints have been evaluated.

- **Baseline incidence rates and demographic data**: The required urban area-specific baseline incidence rates and population data are available for a recent year for at least one of the health endpoints.

- **Geographic heterogeneity**: Because ozone distributions and population characteristics vary geographically across the U.S., we plan to select a set of urban study areas in which each region of the country is represented. We plan to define these regions in such a way as to reflect differences in factors related to ozone distributions, sources, co-pollutants, exposure, and/or effect estimates.

- **Representing areas with relatively larger vulnerable populations**: Baseline incidence rates (e.g., mortality rates) and ozone exposures are higher in some parts of the country than others. We plan to select a set of urban study areas that will include representation of sensitive populations (e.g., those with higher baseline incidence rates of the health effect endpoints being evaluated, lower air conditioning usage which has been related to higher ambient ozone exposures).

- **Consideration of epidemiology studies with more refined exposure metrics**: We plan to include urban study areas for which there is a C-R function estimated using a more refined metric of exposure (e.g., smaller geographic units linked to nearest ozone monitors, rather than constructing a single composite monitor for an entire metropolitan area), where available.

5.3.3 Baseline Health Effects Incidence Data and Demographic Data

As noted earlier (section 5.2.1), the most common epidemiological-based health risk model expresses the reduction in health risk (Δy) associated with a given reduction in ozone concentrations (Δx) as a percentage of the baseline incidence (y). To accurately assess the impact of ozone air quality on health risk in the selected urban areas, information on the baseline incidence of health effects (i.e., the incidence under recent air quality conditions) in each location is needed. Where at all possible, we plan to use county-specific incidences or incidence rates (in combination with county-specific populations). A summary of available baseline incidence data for specific categories of effects is presented below:

- **Availability of baseline incidence data on mortality**: County-specific (and, if desired, age- and race-specific) baseline incidence data are available for all-cause and cause-

specific mortality from CDC Wonder.[1] The most recent year for which data are available online is 2005.[2]

- **Availability of baseline incidence data for hospital admissions and emergency room (ER) visits**:
    - Cause-specific hospital admissions baseline incidence data are available for each of 40 states from the State Inpatient Databases (SID).
    - Cause-specific ER visit baseline incidence data are available for 26 states from the State Emergency Department Databases (SEDD).
    - SID and SEDD are both developed through the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (AHRQ).
    - The data generated from HCUPnet (HCUP's online interactive tool) are state-level summary statistics, whereas the data from the HCUP distributor are at the individual discharge level.
    - In addition to being able to estimate State-level rates, SID and SEDD can also be used to obtain county-level hospital admission and ER visit counts by aggregating the discharge records by county.

EPA is in the process of obtaining the county-specific hospital admission and ER visit baseline incidence data for the most recent single year available for most of the States included in the HCUP data. While we recognize that there is year-to-year variability in baseline incidence data, a single year of data is being obtained due to resource constraints. We plan to examine the potential variability in baseline incidence data and the impact this might have on the risk estimates in sensitivity analyses based on endpoints and locations where we can obtain multi-year baseline incidence data at little or no cost and by examining the variability in baseline incidence rates at the State level.

5.3.4 Assessing Risk In Excess of Policy-Relevant Background

As noted above, staff plans to assess risks associated with ozone concentrations in excess of policy-relevant background concentrations, and to assess risk reductions associated with just

[1] http://wonder.cdc.gov/mortsql.html

[2] Note: For years 1999 – 2005, CDC Wonder uses ICD-10 codes; for years prior to 1999, it uses ICD-9 codes. Since most of the studies use ICD-9 codes, this means that EPA will have to create or find a mapping from ICD-9 codes to ICD-10 codes if the most recent data available are to be used.

meeting current and alternative ozone standards. Following the methods used in the prior ozone risk assessment, risks based on a concentration-response function estimated in an epidemiological or field study will be assessed down to the estimated policy relevant background.

To assess risks associated with ozone concentrations in excess of policy-relevant background concentrations, staff will first calculate the difference between "as is" ozone levels and policy-relevant background. Staff will then calculate the corresponding change in incidence of the health effect associated with that change in ambient ozone concentration. If Δx denotes the change in ozone level from "as is" concentration to the background concentration, then the corresponding change in incidence of the health effect, Δy, for a log-linear concentration-response function (the most common functional form), is

$$\Delta y = y\,[1-e^{-\beta \Delta x}] \qquad (5\text{-}1)$$

where y denotes the baseline incidence and β is the coefficient of ozone in the concentration-response function. A similar calculation would be made if the concentration-response function is of a logistic form.

To assess the risk reduction associated with just meeting the current standard in those locations that do not currently meet this standard, the procedure will be the same, except that in this part of the risk assessment Δx will be the difference between "as is" ozone levels and the ozone levels that will be estimated to exist if the current standards are just met.

To assess the risk reductions associated with just meeting alternative, more stringent standards, above and beyond the risk reductions that would be achieved by just meeting the current standards, Δx will be the difference between ozone levels that will be estimated to exist if the current standards are just met and ozone levels that will be estimated to exist if the alternative, more stringent, standards are just met.

Because the ozone coefficient, β, is estimated rather than known, there is uncertainty surrounding that estimate. This uncertainty is characterized as a normal distribution, with mean equal to the ozone coefficient reported in the study, and standard deviation equal to the standard

error of the estimate, also reported in the study. From this information, staff plans to construct a 95 percent confidence interval around the reported risk or risk reduction (number of cases of the health effect avoided), with that confidence interval primarily reflecting sampling error associated with the underlying effect estimate.[1]

5.4 Characterization of Uncertainty and Variability in the Context of the Ozone Risk Assessment

5.4.1 Overview of Approach for Addressing Uncertainty and Variability

An important component of a population health risk assessment is the characterization of both uncertainty and variability. *Variability* refers to the heterogeneity of a variable of interest within a population or across different populations. For example, populations in different regions of the country may have different behavior and activity patterns (e.g., air conditioning use, time spent indoors) that affect their exposure to ambient ozone and thus the population health response. The composition of populations in different regions of the country may vary in ways that can affect the population response to exposure to ozone – e.g., two populations exposed to the same levels of ozone might respond differently if one population is older than the other. Variability is inherent and cannot be reduced through further research. Refinements in the design of a population risk assessment are often focused on more completely characterizing variability in key factors affecting population risk – e.g., factors affecting population exposure or response – in order to produce risk estimates whose distribution adequately characterizes the distribution in the underlying population(s).

Uncertainty refers to the lack of knowledge regarding the actual values of inputs to an analysis. Models are typically used in analyses, and there is uncertainty about the true values of the parameters of the model (parameter uncertainty) – e.g., the value of the coefficient for ozone in a C-R function. There is also uncertainty about the extent to which the model is an accurate representation of the underlying physical systems or relationships being modeled (model uncertainty) – e.g., the shapes of C-R functions. In addition, there may be some uncertainty surrounding other inputs to an analysis due to possible measurement error—e.g., the values of

[1] The confidence interval will not reflect the impact of other sources of uncertainty such as alternative model choice associated with deriving the effect estimate (although this source of uncertainty may be addressed as part of the sensitivity analysis – see Section 5.4.4).

daily ozone concentrations in a risk assessment location, or the value of the baseline incidence rate for a health effect in a population.[1] In any risk assessment, uncertainty is, ideally, reduced to the maximum extent possible through improved measurement of key variables and ongoing model refinement. However, significant uncertainty often remains, and emphasis is then placed on characterizing the nature of that uncertainty and its impact on risk estimates. The characterization of uncertainty can be both qualitative and, if a sufficient knowledgebase is available, quantitative.

The characterization of uncertainty associated with risk assessment is often addressed in the regulatory context using a tiered approach in which progressively more sophisticated methods are used to evaluate and characterize sources of uncertainty depending on the overall complexity of the risk assessment (WHO, 2008). Guidance documents developed by EPA for assessing air toxics-related risk and Superfund Site risks (U.S. EPA, 2004 and 2001, respectively) as well as recent guidance from the World Health Organization (WHO, 2008) specify multitier approaches for addressing uncertainty.

For the ozone risk assessment, as noted above in section 5.1, we are planning to use a tiered framework developed by WHO to guide the characterization of uncertainty. The WHO guidance presents a four-tiered approach, where the decision to proceed to the next tier is based on the outcome of the previous tier's assessment. The four tiers described in the WHO guidance include:

- **Tier 0:** recommended for routine screening assessments, uses default uncertainty actors (rather than developing site-specific uncertainty characterizations);
- **Tier 1:** the lowest level of site-specific uncertainty characterization, involves qualitative characterization of sources of uncertainty (e.g., a qualitative assessment of the general magnitude and direction of the effect on risk results);
- **Tier 2:** site-specific deterministic quantitative analysis involving sensitivity analysis, interval-based assessment, and possibly probability bound (high- and low-end) assessment; and

[1] It is also important to point out that failure to characterize variability in an input used in modeling can also introduce uncertainty into the analysis. This reflects the important link between uncertainty and variability with the effort to accurately characterize variability in key model inputs actually reflecting an effort to reduce uncertainty.

- **Tier 3:** uses probabilistic methods to characterize the effects on risk estimates of sources of uncertainty, individually and combined.

With this four-tiered approach, the WHO framework provides a means for systematically linking the characterization of uncertainty to the sophistication of the underlying risk assessment. Ultimately, the decision as to which tier of uncertainty characterization to include in a risk assessment will depend both on the overall sophistication of the risk assessment and the availability of information for characterizing the various sources of uncertainty.

The risk assessment to be completed for the ozone NAAQS review is relatively complex, thereby warranting consideration of a full probabilistic (WHO Tier 3) uncertainty analysis. However, we anticipate that limitations in available information will likely prevent this level of analysis from being completed. In particular, the incorporation of uncertainty related to key elements of C-R functions (e.g., competing lag structures, alternative functional forms, etc.) into a full probabilistic WHO Tier 3 analysis would require that probabilities be assigned to each competing specification of a given model element (with each probability reflecting a subjective assessment of the probability that the given specification is the "correct" description of reality). However, for many model elements we expect that there will be insufficient information on which to base these probabilities. One approach that has been taken in such cases is expert elicitation; however, this approach is resource- and time-intensive and consequently, it is not feasible to use this technique in support of the ozone risk assessment.[1]

For most elements of this risk assessment, rather than conducting a full probabilistic uncertainty analysis, we do expect to include a qualitative discussion of the potential impact of uncertainty on risk results (WHO Tier1) and/or completed sensitivity analyses assessing the potential impact of sources of uncertainty on risk results (WHO Tier 2). In conducting sensitivity analyses, we are planning to use both single- and multi-factor approaches (to look at the individual and combined impacts of sources of uncertainty on risk estimates). In addition, in

[1] Note, that while we anticipate that a full probabilistic uncertainty analysis will not completed for this risk assessment, we are expecting to use confidence intervals associated with effects estimates (obtained from epidemiological studies) to incorporate statistical uncertainty associated with sample size considerations in the presentation of risk estimates. Technically, this type of probabilistic simulation represents a Tier 3 uncertainty analysis, although as noted here, it will be limited and only address uncertainty related to the fit of the C-R functions.

conducting sensitivity analyses, we expect to use only those alternative specifications for input parameters or modeling approaches that are deemed to have scientific support in the literature (and so represent alternative reasonable input parameter values or modeling options). This means that, as discussed earlier in section 5.1, the alternative risk results generated in the sensitivity analyses are expected to represent reasonable risk estimates that can be used to provide a context, with regard to uncertainty, within which to assess the set of core (base case) risk results. Potential sources of uncertainty included in the sensitivity analysis are presented below in section 5.3.4.

The remainder of this section discusses how we are planning to address variability and uncertainty within the ozone NAAQS risk assessment. The treatment of variability is discussed first (section 5.4.2) by identifying sources of variability associated with the modeling of ozone-related risk and noting which of those sources are reflected in the risk modeling approach presented here. Next, the treatment of uncertainty is addressed, which will include both a qualitative and quantitative component. The qualitative component is described first (section 5.4.3), including plans for identifying and describing key sources of uncertainty, and noting whether those sources of uncertainty are addressed quantitatively in the risk assessment model. A preliminary list of key sources of uncertainty for the risk assessment is provided as part of this discussion. The quantitative component of the uncertainty characterization approach, which is structured around single-factor and multi-factor sensitivity analysis methods, is then described (section 5.4.4). The representativeness analysis planned to support interpretation of the urban study area-level risk estimates is discussed in section 5.4.5.

5.4.2 Addressing Variability

Key sources of variability associated with the modeling of population-level risk associated with ozone exposure are presented below, including whether, and to what extent, we plan to address each source of variability:

- **Spatial gradients in ozone (and related population exposure)**: This source of variability is likely to be less-well captured in the risk assessment primarily because the majority of epidemiological studies providing effect estimates are themselves limited in reflecting more detailed patterns of ozone exposure among populations. More

specifically, the epidemiological studies typically use an average ambient concentration developed across population-oriented monitors as a surrogate for exposure. Note, however that the exposure assessment described in Chapter 3 may allow this issue to be investigated to some degree, particularly as it impacts on exposure error misclassification in the epidemiological studies underpinning the C-R functions used in this risk assessment. In addition, a few epidemiological studies being considered for inclusion in this analysis include more refined characterization of population-level exposure (e.g., based on more spatially differentiated linkages between population-level monitors and segments of the study population). We plan to consider the use of those studies with more refined population exposure characterization to examine the issue of spatial gradients in ozone and demographics and the degree to which this source of variability impacts risk estimates.

- **Demographics (i.e., greater concentrations of susceptible populations in certain locations)**: We plan to include multiple urban study areas reflecting differences in demographics in different regions of the country to address this issue. In addition, as noted in the previous bullet, we plan to consider studies with more refined characterization of population-level exposure, to provide insights into the degree to which this source of variability impacts risk estimates.

- **Behavior related to ozone exposure (e.g., outdoor time, air conditioning use)**: We plan to include multiple urban study areas reflecting differences in a variety of factors related to ozone exposure (e.g., time spent outdoors, air conditioner use, housing stock, which can affect ozone infiltration, and commuting patterns).

- **Susceptibility to specific populations to ozone exposure** (note – this could include a number of factors e.g., magnitude of the effect estimate, underlying health status): We plan to consider this source of variability by using effect estimates and lag structures specific to each urban study location.

- **Differences in baseline incidence of disease**: This source of variability would potentially be captured through the use of localized baseline incidence data (e.g., county-level).

- **Longer-term temporal variability in ambient ozone levels** (reflecting meteorological trends, as well as future changes in the mix of ozone sources and regulations affecting ozone): This is more difficult to incorporate into the analysis and reflects a combination of variability as well as uncertainty.

5.4.3 Uncertainty Characterization – Qualitative Assessment

As noted in section 5.4.1, we are planning to base the uncertainty analysis carried out for this risk assessment on the framework outlined in the WHO guidance document (WHO, 2008). That guidance calls for the completion of a Tier 1 qualitative uncertainty analysis, provided the initial Tier 0 screening analysis suggests the-re is concern that uncertainty associated with the analysis is sufficient to significantly affect risk results (i.e., to potentially affect decision making based on those risk results). Ozone risk assessments completed for previous NAAQS reviews have clearly identified sources of uncertainty that could have significant impacts on risk estimates, thereby allowing us to skip a Tier 0 assessment and proceed directly to a Tier 1 analysis (i.e., a qualitative discussion of potential sources of uncertainty including an assessment of the nature, magnitude and potential direction of impact of each source of uncertainty on the core risk estimates). A preliminary list of potentially important sources of uncertainty likely to be included in a Tier 1 assessment has been developed for this plan and is presented below (note, some of these sources may be addressed in the quantitative uncertainty analysis, when feasible):

- **Procedure for characterizing recent air quality for urban study areas**: There is uncertainty associated with characterizing recent air quality conditions at individual urban study areas. This uncertainty is reflected in the number of decisions or options that must be considered in designing an approach for characterizing recent air quality including: (a) whether to rely on monitoring data or to combine it with modeling data, (b) how to match ambient ozone levels to potentially exposed populations from a spatial standpoint (e.g., use a single composite monitor or a more differentiated polygon-based exposure surface, and (c) if a composite monitor approach is used, whether to design that composite monitor to most closely match the way monitoring data were used in the underlying epidemiological study providing the C-R function or design it to be more representative of potentially current exposures (e.g., weight it by activity profiles simulated for the current population).

- **Procedures for adjusting air quality to simulate alternate standard levels:** There is uncertainty in developing the method for adjusting current ambient ozone levels (at individual monitors used in the risk assessment) to simulate just attaining alternative standard (methods available are likely to include both retrospective empirical monitor-based trend analysis and forward-looking model-based predictions – see section 3.2.1 and section 2.3 for additional detail).

- **Estimates of policy-relevant background ozone levels in a particular location**. There is uncertainty associated with characterizing background for individual locations (see Section 5.2.2 for additional detail).

- **The impact of historical air quality on estimates of health risk from long-term ozone exposures** (i.e., the amount of time that a population experiences new lower ambient ozone levels before there is a noticeable reduction in health effect incidence): Some studies of long-term mortality provide effect estimates differentiated by consecutive, multi-year time periods. These studies may provide insights into this issue and the degree to which it could affect risk estimates (by providing different effect estimates).

- **Statistical uncertainty associated with the fit of the C-R function**.

- **Shape of the C-R function:** Of particular concern is uncertainty related to the shape of the C-R function at lower exposure levels.

- **Potential role of co-pollutants and different lag structures**: these are related to the C-R function (and nature of the associated effects estimate).

- **Transferability of C-R functions from study locations to urban study area locations**: this reflects variation in (a) ozone distributions, (b) the possible role of copollutants in influencing risk, (c) relationship between ambient ozone and actual exposure, and (d) differences in population characteristics. However, it is anticipated that the transferability issue will play less of a role in the upcoming analysis, since studies used to derive C-R functions will often be matched to our urban study area locations. However, there may still be transferability issues arising from changes in these factors between the time period when the C-R functions were estimated and the time period of this risk analysis.

5.4.4 Uncertainty Characterization – Quantitative Analysis

In addition to the Tier 1 qualitative assessment of uncertainty discussed in the previous section, we are also anticipating that we will complete a Tier 2 assessment of uncertainty, which involves application of deterministic methods including sensitivity analysis and bounding analyses.[1] For this ozone risk assessment, we are planning to focus primarily on single and multi-factor sensitivity analyses which are intended to (a) help identify which uncertainty factors (acting either alone, or in concert with other factors) have a significant impact on the core risk

[1] As noted earlier, uncertainty related to the statistical fit of the C-R functions will be addressed using probabilistic simulation to derive confidence intervals around the core risk estimates (i.e., a Tier 3 probabilistic approach towards characterizing the impact of uncertainty on core risk estimates).

estimates and (b) generate an alternative reasonable set of risk estimates that supplement the core risk estimates and involve overall consideration of uncertainty in the risk estimates.[1] This quantitative uncertainty analysis would likely focus on a subset of the sources of uncertainty identified above for the Tier 1 assessment with this subset reflecting sources of uncertainty for which we can clearly identify competing datasets or modeling approaches with some degree of support in the literature. Table 5-1 identifies those modeling elements that are being considered for inclusion in the sensitivity analysis and includes identification of the options for each modeling element that could be considered in the sensitivity analysis. Note, that in each case, one of these options will likely be identified for the core analysis, with the remaining option(s) either (a) being included as sensitivity analyses, or (b) discussed qualitatively as part of the overall uncertainty analysis. However, we are not prepared at this stage in the planning process to identify core versus sensitivity analysis options, or to specific which alternative approaches will be included in the quantitative sensitivity analysis versus covered qualitatively.

The step-wise procedure for conducting the deterministic uncertainty analysis is illustrated in Figure 5-2. It is important to point out that we plan to generate a core set of risk estimates prior to conducting the uncertainty analysis. This core set of risk estimates would be derived by first applying the criteria discussed in preceding sections (sections 5.2 and 5.3) to identify those options for key modeling elements which have the strongest scientific support (with these determinations being based primarily on the evaluation provided in the ISA).[2] The core set of risk estimates will be generated for each combination of urban study area and air quality scenario.

[1] As noted earlier, ideally, we would also include a 2-dimensional probabilistic analysis of uncertainty and variability (i.e., a Tier 3 assessment in the WHO framework), since this would allow us to provide a more complete and integrated characterization of uncertainty and variability associated with risk estimates. However, limitations in our ability to assign rigorous and defensible confidence levels to competing modeling approaches and input datasets is expected to prevent us from completing this type of analysis.

[2] For example, as noted in section 5.3.1, if a study provides both single-day and distributed lag models, the distributed lag model would be used in the core analysis, while the individual day lags, if retained in the risk assessment, would be included in the uncertainty analysis. With regard to non-linearity in functions, including the potential for thresholds, generally non-threshold models will be used in the core analysis (based on information provided in the ISA) and thresholds models, if they are considered at all, would be reserved for the uncertainty analysis. It is also important to point out that for some of the modeling elements, multiple options may be included as part of the core simulation (e.g., both multi- and single-component models may be used in core simulations for specific health endpoints).

Table 5-1. Planned Sensitivity Analyses for the Epidemiologic-Based Risk Assessment

Component of the Risk Assessment	Options Potentially Considered for the Sensitivity Analysis (Note, these include all options identified for a particular component or modeling element – one of the identified options will likely be identified for the core analysis, with the remainder being included in the sensitivity analysis)
Air quality	
Characterization of recent air quality at urban study areas	• use of composite monitors (or other aggregations of monitors) that are linked to the method used for representing ambient ozone levels in the underlying epidemiological studies providing the C-R functions, • use of a composite monitor approach that weights monitors by their contribution to population exposure (as reflected in microenvironmental exposure modeling) rather than matching structure to approach used in underlying epidemiological studies • use of model-monitor fused surfaces. Note, that these alternative methods for characterizing current air quality may only be assessed at a subset of urban study areas as part of the sensitivity analysis.
Background concentrations	• use monitor data alone, or in combination with modeling data, • whether to use composite monitors or a more spatially-differentiated exposure surface.
Key design element associated with air quality sensitivity analysis	As noted in section 2.2 and 5.1, a key aspect of designing the approach for characterizing air quality (including core and sensitivity analyses) is consideration for the degree of spatial heterogeneity in monitored ozone levels. If the spatial gradient within a study area in ozone levels is not that substantial, reflecting the dominance of secondary formation for ozone, than there may be little utility in considering varied approaches for deriving exposure surrogates and conducting rollbacks (i.e., in a study area with fairly uniform ozone levels at a given point in time, alternative approaches for these modeling steps may not produce meaningfully different results). Conversely , if a study area does have significant spatial heterogeneity in ozone levels, then the approach used to characterize current ozone levels and link it to population and the approach used to conduct rollback could have a notable impact on risk estimates.

Selection of health effect endpoint categories (and endpoints)	
Health effect endpoints to model	As noted in section 5.3, the core analysis will focus on endpoints contained within health effect endpoint categories assigned a causal or likely causal association with ozone exposure. The Sensitivity Analysis may include endpoints (e.g., developmental) that are assigned a suggestive of casual association classification. As noted in section 5.3, the specific category of long-term exposure-related respiratory mortality (if modeled), may be included in the core analysis, or as part of the Sensitivity Analysis depending on how the degree of support for an association with ozone exposure is ultimately assessed.
Exposure-response functions	
Extrapolation below lowest levels of exposure used in studies	• Extend model without modification below lowest exposure level • Extend model to the lowest exposure level reflected in the underlying epidemiologic study (with this reflecting a higher-confidence calculation) • Consider alternate model forms for points below lowest exposure level (if there is some rationale for this supported by study data, including toxicological information). • Consideration for thresholds (only for long-term exposure-related endpoints).
Consideration for alternative C-R functions reflecting different model constructs (e.g., single vs. multi-pollutant functions, single vs. multi city studies)	As noted in section 5.3.1, if an epidemiological study provides multiple functions reflecting for example, a single versus multi-pollutant model, we will include both forms. Looking more broadly, we will also include C-R functions (for a given endpoint) from single and multi-city studies given the strengths afforded by each (assuming that each study meets criteria for a sound analysis).
Bayesian-adjusted county-level estimates from multi-city short-term studies	Consideration for impact of using county-level Bayesian-adjusted C-R functions (extracted form multi-city short-term studies) versus application of the national-level effect estimates originally provided by these multi-city studies.
Baseline Incidence	
Aggregation scale	Consideration for more aggregate baseline incidence data (national, state, etc.) versus county-specific information in the county with the best local baseline incidence data

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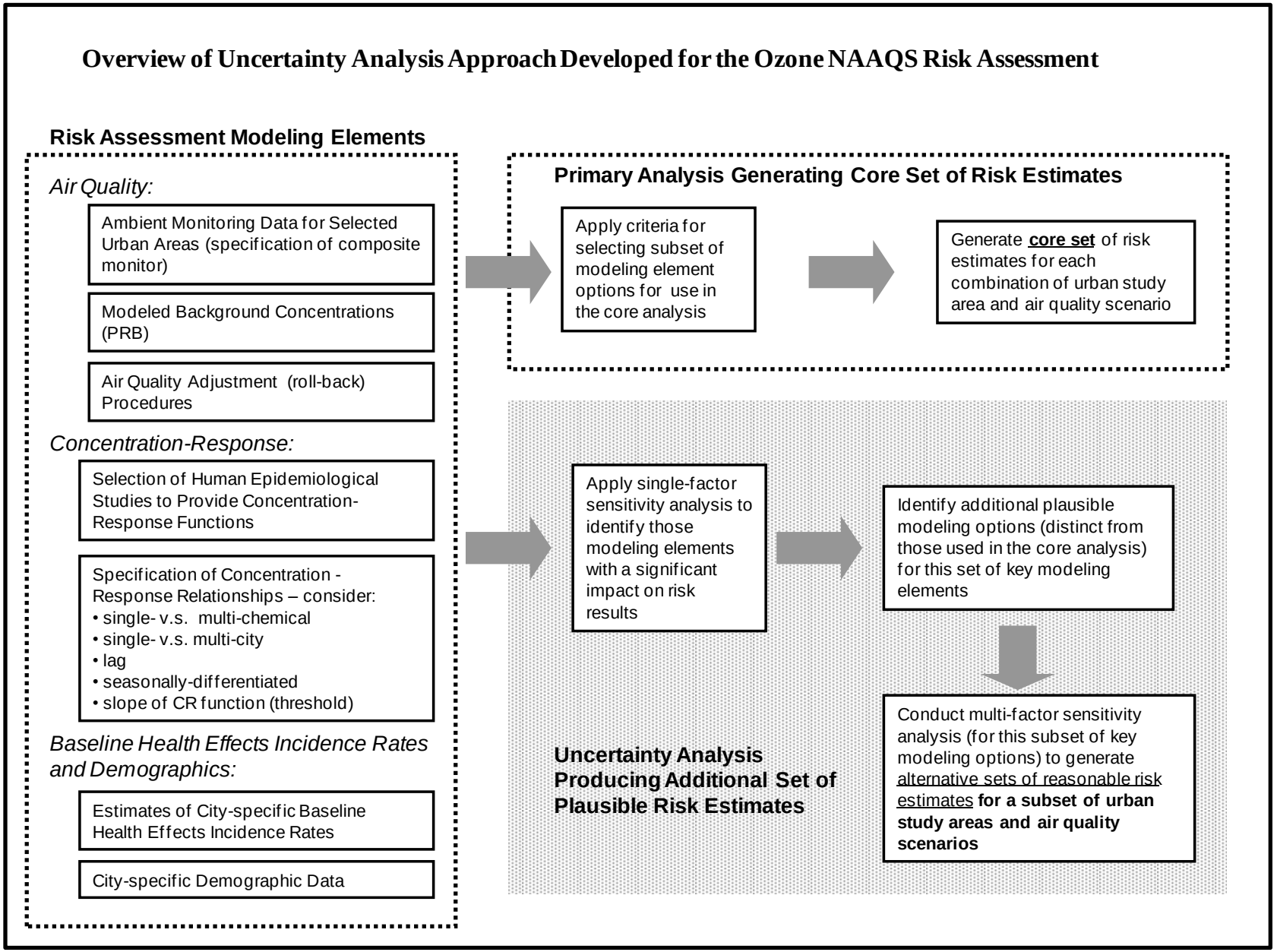

Figure 5-2. Overview of Approach For Uncertainty Analysis of Risk Assessment Based on Epidemiologic Studies

Once the core set of risk estimates has been generated, the uncertainty analysis will begin with a single-factor sensitivity analysis intended to identify those modeling elements (comprising the ozone risk assessment framework) that have the potential to significantly impact risk estimates. This set of key modeling elements would form the basis for the uncertainty analysis. Next, plausible modeling options (distinct from those used in the core analysis) would be specified for each of these key modeling elements. In identifying these plausible modeling options, we plan to place emphasis on identifying input factors or modeling approaches, which, while representing alternatives to those used in the core simulation, still have some degree of scientific support in the literature. Consequently, while we may have less confidence in risk estimates generated using these alternate modeling options relative to the core risk estimates, they could still considered reasonable and consequently may be interpreted as providing additional perspective on overall uncertainty associated with the core set of risk estimates.

Once the set of plausible modeling options is specified for the key modeling elements, we plan to use a multi-factor sensitivity analysis to generate a set of reasonable alternative risk estimates. Specifically, various combinations of these alternative modeling options would be used to generate risk estimates, each representing an uncertainty simulation.[1] We plan to generate this set of alternative risk estimates for a subset of the urban study areas and air quality scenarios.

The combined sets of core results and alternative risk estimates (for a combination of urban study area and air quality scenario) could be interpreted as representing an initial characterization of risk for that combination of urban study area and air quality scenario, reflecting recognized sources of uncertainty in risk modeling. However, this interpretation needs to be tempered by consideration of several factors: (a) this does not represent a characterization of a distribution of uncertainty around the core set of risk estimates, it merely represents several point estimates likely falling within that uncertainty distribution and (b) the set of modeled risk estimates may not contain actual upper-bound and lower-bound risk estimates given scientifically defensible modeling options. Despite these caveats, the risk estimates defined by

[1] Note, that care would be taken in linking these modeling options together to insure that they are compatible and do not represent combinations that are scientifically not defensible.

the sets of core and alternative risk estimates should be useful to characterize confidence associated with the results of the application of the ozone risk assessment model.

5.4.5 Representativeness Analysis

As discussed in section 5.1, we are planning to complete a representativeness analysis designed to support the interpretation of risk estimates generated for the set of urban study areas included in the risk assessment. The representativeness analysis will focus on comparing urban study area-level values to national-scale distributions for key ozone-risk related attributes (e.g., demographics including socioeconomic status, air-conditions use, baseline incidence rates and ambient ozone levels). The goal, with these comparisons will be to assess the degree to which the urban study areas provide coverage for different regions of the country as well as for areas of the country likely to experience elevated ozone-related risk due to their specific mix of attributes related to ozone risk.

The national-scale distributions of ozone risk-related parameters would be specified at the country-level and would be based on generally available data, e.g. from the 2000 Census, CDC, or other sources. The specific values of these parameters for the selected urban study areas would then be plotted on these national-scale distributions, and an evaluation of how representative the selected study areas are of the individual parameters, relative to the national distributions, could be completed. The specific choices of parameters for which we would examine the representativeness of the selected urban study areas would be informed through an assessment of the epidemiology literature. We plan to particularly focus on meta-analyses and multi-city studies which have identified parameters that influence heterogeneity in ozone effect estimates, and exposure studies which have explored determinants of differences in personal exposures to ambient ozone. While personal exposure is not generally incorporated directly into epidemiology studies evaluating ambient ozone-related effects, differences in the ozone effect estimates between cities clearly is impacted by differing levels of those exposure determinants. Once we have identified these parameters, we plan to develop city-specific distributions for those parameters (or reasonable surrogates) based on readily available data sources. Formal comparisons of parameter distributions for the set of urban study areas and the city-specific parameter distributions using standard statistical tests (e.g. the Kolmogorov-Smirnov test for

equality of distributions) would not be useful in this context, since we are more interested in meaningful differences than statistical significance. Therefore, we plan to use graphical comparisons using probability density functions, cumulative distribution functions, and boxplots.

As noted in section 5.1, as part of the representativeness analysis, we are also considering generating national-scale ozone mortality estimates (based both on long-term and short-term exposure). In the context of both short-term and long-term exposure-related mortality, these national-level estimates could be used to assess the degree to which our urban study areas capture urban areas across the U.S. that potentially experience the greatest ozone-related mortality. For long-term mortality, we would consider a national-scale assessment conducted at the county-level using the same national-level effect estimate obtained from the cohort study used in modeling each urban study area (with this assessment likely focusing on respiratory mortality, as discussed above and in section 5.1). For short-term exposure-related mortality, rather than generating a comprehensive national-estimate that has full coverage (i.e., covers all counties in the U.S.), we would likely model the set of urban areas included in the time series study that provided the effect estimates used in the primary estimate of short-term mortality generated for our urban study areas (i.e., we would model mortality for each of the urban study areas included in the underlying time series study). While the mortality estimate for short-term exposure would not be truly national (in that it would not cover all counties in the country), by including most of the larger urban areas in the U.S. it would provide close to a national estimate.

6 PRESENTATION OF RISK ESTIMATES TO INFORM CONSIDERATION OF STANDARDS

This section discusses the nature of the risk estimates that we plan to generate as part of the review of the ozone NAAQS. We plan to conduct the risk assessment in two phases. Phase 1 would include analysis of risk associated with recent air quality and simulating air quality to just meet the current NAAQS. Phase 2 would focus on evaluating risk associated with simulating air quality that just meets alternative NAAQS under consideration.

We plan to present risk estimates in two ways: (1) total (absolute) health effects incidence (above background) for recent air quality and simulations of air quality just meeting the current and alternative NAAQS under consideration, and (2) risk reduction estimates, reflecting the difference between (a) risks associated with recent air quality compared to risks associated with just meeting the current NAAQS and (b) reflecting the difference between risks associated with just meeting the current NAAQS compared to risks associated with just meeting alternative NAAQS under consideration.

In presenting risk estimates, we plan to emphasize the core (base-case) estimates given that these would include risk estimates with greater overall confidence. We plan to also present additional risk estimates generated as part of the uncertainty analyses in order to provide additional context for understanding the potential impact of uncertainty on the risk estimates and particularly on the core estimates of risk. The results of the representativeness analysis (discussed in section 5.4.5) would likely be presented using a combination of (a) cumulative probability plots (for the national-level distribution of ozone risk-related parameters) with the locations where the individual urban study areas fell within those distributions noted in the plots and (b) box and whisker plots, again contrasting the national-scale distribution of the ozone risk-related parameters with the values for individual urban study areas. Similar types of plots would be used to present national-scale mortality estimates (should they be generated); contrasting them with estimates generated for individual urban study areas.

7 SCHEDULE AND MILESTONES

The Integrated Review Plan provides an overview of ozone review schedule. Table 7-1 below includes the key milestones for the exposure analysis and health risk assessment that will be conducted as part of the current ozone NAAQS review. A consultation with the CASAC Ozone Panel is planned for May 19-20, 2011 to obtain input on this draft Scope and Methods Plan. Staff will then proceed to develop exposure and health risk estimates associated with recent ozone levels and levels adjusted to just meet the current 8-hour ozone standard. These estimates and the methodology used to develop them will be discussed in the first draft ozone exposure analysis and health risk assessment. This draft report will be released for CASAC and public review in October 2011. EPA will receive comments on these draft documents from the CASAC Ozone Panel and general public at a meeting in November 2011. The revised exposure analysis and risk assessment reports will include estimates associated with just meeting any alternative standards that may be recommended by staff for consideration. The revised analyses will be released in May 2012 for review by CASAC and the public at a meeting to be held in July 2012. Staff will consider these review comments and prepare a final exposure analysis and risk assessment report by October 2012.

Table 7-1. Key Milestones for the Exposure Analysis and Health Risk Assessment for the Ozone NAAQS Review

Milestone	Date
First Draft Integrated Science Assessment (ISA)	March 2011
Scope and Methods Plan for the Exposure Analysis and Health Risk Assessment	April 2011
CASAC/public review and meeting on First Draft ISA	May 19-20, 2011
CASAC consultation on Scope and Methods Plan	May 19-20, 2011
Second Draft ISA	September 2011
First Draft Exposure Analysis and Risk Assessment	October 2011
CASAC/public review and meeting on Second Draft ISA and First Draft Exposure Analysis and Risk Assessment	November 2011
Final ISA	February 2012
Second Draft Exposure Analysis and Risk Assessment	May 2012
First Draft Policy Assessment	June 2012

CASAC/public review and meeting on Second Draft Exposure Analysis and Risk Assessment and First Draft Policy Assessment	July 2012
Final Exposure Analysis and Risk Assessment	October 2012
Second Draft Policy Assessment	November 2012
CASAC/public review of Second Draft Policy Assessment	January 2013
Final Policy Assessment	March 2013
Proposed Rulemaking	September 2013
Final Rulemaking	June 2014

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