Ozone Health Assessment Plan: Scope and Methods for Exposure Analysis and Risk Assessment

Draft

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DISCLAIMER

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Ozone Health Assessment Plan: Scope and Methods for Exposure Analysis and Risk Assessment

1 INTRODUCTION

The U.S. Environmental Protection Agency (EPA) is presently conducting a review of the national ambient air quality standards (NAAQS) for ozone (O_3). 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 which 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 O_3 NAAQS review is presented in a *Plan for Review of the National Ambient Air Quality Standards for Ozone* (EPA, 2005a), which is available at: http://www.epa.gov/ttn/naaqs/standards/ozone/s_o3_cr_pd.html . That plan discusses the preparation of two key documents in the NAAQS review process: an Air Quality Criteria Document (AQCD) and a Staff Paper. The AQCD provides a critical assessment of the latest available scientific information upon which the NAAQS are to be based, and the Staff Paper evaluates the policy implications of the information contained in the AQCD and presents staff conclusions and recommendations for standard-setting options for the Administrator to consider. In conjunction with preparation of the Staff Paper, staff in EPA's Office of Air Quality Planning and Standards (OAQPS) conducts various policy-relevant assessments, including in this review a quantitative exposure analysis and a human health risk assessment. This draft document describes the scope and methods that staff is planning to use for these assessments. The final section of this scope and methods plan identifies the major milestones and interim steps involved in the planning, conduct, and documentation of these assessments.

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[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."

1.1 Purpose of Scope and Methods 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 O_3 under existing air quality levels ("as is" exposures and health risks), upon attainment of the current O_3 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 O_3 Staff Paper.

The planned O_3 exposure analysis and health risk assessment address short-term exposures to O_3 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 are insufficient information to develop quantitative risk estimates. Staff plans to discuss these additional health endpoints qualitatively in the O_3 Staff Paper. The risk assessment is intended as a tool that, together with other information on these health endpoints and other health effects evaluated in the O_3 AQCD and O_3 Staff Paper, 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.

1.2 Background

As part of the last O_3 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; Johnson, 1997) that describe these analyses can be found at: http://www.epa.gov/ttn/naaqs/standards/ozone/s_o3_pr_td.html. EPA also conducted a health risk assessment that produced risk estimates for the number of children and percent of children experiencing lung function and respiratory symptoms associated with the exposures estimated for these same 9 urban areas. This portion of the risk assessment was based on exposure-response relationships developed from analysis of data from several controlled human exposure studies. The risk assessment for the last review also included risk estimates for excess respiratory-related hospital admissions related to O_3 concentrations for New York City based on a concentration-response relationship reported in an epidemiology study. Risk estimates for lung function decrements, respiratory symptoms, and hospital admissions were developed for "as is" air quality and for just meeting the existing 1-hour standard and several alternative 8-hour standards. Reports describing the health risk assessment (Whitfield et al., 1996; Whitfield, 1997) can be found at: http://www.epa.gov/ttn/naaqs/standards/ozone/s_o3_pr_td.html.

The planned exposure analysis and health risk assessment described in this Scope and Methods Plan build upon the methodology and lessons learned from the exposure and risk work

conducted for the last review. These plans are also based on the information currently available in the first draft O_3 AQCD; as such, some aspects of these plans may change based on changes that may be incorporated in the final O_3 AQCD.

2 AIR QUALITY CONSIDERATIONS

Staff plans to perform exposure and health risk analyses using the most recent year (2004) of air quality data available at this time. The time period to be analyzed will be the O_3 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.

The following air quality scenarios will be considered:

- "As is" air quality in each urban area for 2004,
- meeting the current 8-h 0.08 ppm, average 4th daily maximum standard, and
- meeting alternative O_3 standards.

In order to conduct exposure and risk analyses for the last two scenarios, staff will adjust the air quality data to simulate just meeting the current and alternative standards. The adjustment of air quality data will be based on three years of data (2002 - 2004). Staff is currently considering various approaches to making such adjustments, including the quadratic air quality adjustment approach that was evaluated and used in the last review (Johnson, 1997).

A key issue to be addressed in the O_3 Staff Paper is the characterization of policy-relevant background O_3 levels in the U.S, which is defined as the distribution of O_3 concentrations that would be observed in the U.S. in the absence of anthropogenic (man-made) emissions of O_3 precursors in the U.S., Canada, and Mexico. This definition appropriately 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. Staff estimates of policy-relevant background, including consideration of regional and seasonal differences, will be informed by information and analyses in the draft O_3 AQCD, consideration of the results of air quality simulation models, and analyses of measured ambient O_3 concentrations. In particular, the results of the global tropospheric O_3 model GEOS-CHEM will be used to estimate monthly average background O_3 levels for different geographic regions across the U.S. These GEOS-CHEM simulations include a background simulation in which North American anthropogenic emissions of nitrogen oxides, non-methane volatile organic compounds, and carbon monoxide are set to zero, as described in Fiore et al. (2003).

3 SCOPE AND APPROACH FOR POPULATION EXPOSURE ANALYSIS

3.1 Overview

Population exposure to ambient O_3 levels will be evaluated using a new version of the Air Pollutants Exposure (APEX) model, also referred to as the Total Risk Integrated Methodology/Exposure (TRIM.Expo) model. Exposure estimates will be developed for current O_3 levels, based on 2004 air quality data, and for O_3 levels associated with just meeting the current 8-h O_3 NAAQS and alternative O_3 standards, based on adjusting 2002-2004 air quality data. Exposure estimates will be modeled for 12 urban areas located throughout the U.S. for 1) the general population, 2) all school-age children, 3) active school-age children, and 4) asthmatic school-age children. 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. The methodology used to conduct the exposure analysis as well as summary results and key findings from the exposure analysis will be presented in the O_3 Staff Paper. In addition, an exposure analysis technical support document with a more detailed description of the methodology and results will accompany the O_3 Staff Paper.

3.2 The Population Exposure Model

The EPA has developed APEX as a tool for estimating human population exposure to criteria and air toxic pollutants. APEX serves as the human inhalation exposure model within the Total Risk Integrated Methodology[2] (TRIM) framework (Richmond et al., 2002; EPA 2003). APEX is a PC-based model that was derived from the probabilistic NAAQS Exposure Model (pNEM) used in the last O_3 NAAQS review (Johnson et al., 1996a, 1996b). Figure 1 provides a schematic overview of the APEX model.

APEX simulates the movement of individuals through time and space and their exposure to a given pollutant in indoor, outdoor, and in-vehicle microenvironments. The model stochastically generates simulated individuals using census-derived probability distributions for demographic characteristics (Figure 1, steps 1-3). The population demographics are from the 2000 Census at the tract level, and a national commuting database based on 2000 census data

[2] The Total Risk Integrated Methodology is described at http://www.epa.gov/ttn/fera.

provides home-to-work commuting flows between tracts. Any number of simulated individuals can be modeled, and collectively they represent a random sample of the study area population.

Diary-derived time activity data from the Consolidated Human Activity Database (CHAD) (McCurdy et al., 2000; EPA, 2002; Graham and McCurdy, 2004) are used to construct a sequence of activity events (each event $\leq$ 60 minutes) for each simulated individual consistent with the individual's demographic characteristics and accounting for effects of day type and temperature on daily activities (Figure 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 by hour to obtain a continuous time series of hourly exposures spanning the time period of interest (Figure 1, steps 5, 6).

APEX has a flexible approach for simulating microenvironmental concentrations, where the user can define the microenvironments to be modeled. For the application to O_3, the following microenvironments will be modeled:

- Indoors - residence
- Indoors - bars and restaurants
- Indoors - schools
- Indoors - day care centers (commercial)
- Indoors – other (e.g., offices, shopping)
- Outdoors - near road
- Outdoors – other (e.g., playgrounds, parks)
- In vehicle - cars, trucks, etc.
- In vehicle - mass transit vehicles

The concentrations in each microenvironment are calculated using either a factors or mass-balance approach, and the user specifies the probability distributions of the parameters that go into the concentration calculations (e.g., indoor-outdoor air exchange rates). These distributions can depend on the values of other variables in the model. For example, the distribution of air exchange rates in a home, office, or car depends on the type of heating and air conditioning present, which are also stochastic inputs to the model. The user can choose to keep the value of a stochastic parameter constant for the entire simulation (e.g., house volume), or can specify that a new value shall be drawn hourly, daily, or seasonally from specified distributions. APEX also allows the user to specify diurnal, weekly, or seasonal patterns for various microenvironmental parameters.

The calculation of microenvironmental concentrations in APEX is dependent not only on the parameter distributions for the mass balance and factors approaches, but also on the ambient (outdoor) O_3 concentrations and temperatures. Hourly O_3 concentration measurements from the fixed-site monitoring data maintained in EPA's Air Quality System and surface temperatures from the National Weather Service will be spatially interpolated for each study area for input to APEX.

Exposure modeling will be conducted based on O_3 concentrations measured in 2004 and for air quality scenarios reflective of meeting alternative O_3 standards. Exposure modeling will also be performed based on policy-relevant background concentration levels alone, in order to be able to assess health risks due to O_3 concentrations in excess of background.

3.3 Use of Human Activity Data

3.3.1 Longitudinal human activity data

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 average subject in the time/activity studies provided less than two days of diary data. For this reason, the construction of a season-long activity sequence for each individual requires some combination of repeating data from one subject and using data from multiple subjects. A key issue in this assessment is the development of an approach for creating O_3-season or year-long activity sequences for individuals based on a cross-sectional activity data base that includes 24-hour records. 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. Staff, in conjunction with staff from NERL, is developing a methodology for constructing longitudinal diaries from the CHAD data which will be used in the O_3 exposure analysis. This method will be described in the exposure analysis technical support document.

3.3.2 Representativeness of activity data

The CHAD includes data from several surveys covering specific time periods at city, state, and national levels, with varying degrees of representativeness. NERL staff plans to supplement these data with more recent data where available.[3] The extent to which the human activity database provides a balanced representation of the population being modeled is likely to vary 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 is unlikely to fully account for all intercity differences in people's activities. Activity patterns are likely to be affected by many local factors, including topography, land use, traffic patterns, mass transit systems, and recreational opportunities. Issues related to the selection and representativeness of the CHAD activity diaries for the 12 urban areas modeled will be addressed in the exposure analysis technical support document and in the O_3 Staff Paper.

[3] For example, the time diary activity data from the 2002 Child Development Supplement (CDS-II) are available at http://psidonline.isr.umich.edu/Data. This survey collected activity data for one randomly sampled weekday and one weekend day for 2,569 children and has more than 99,000 activity records.

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-h average O_3 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 O_3 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 O_3 season that an individual is exposed to the exposure indicator of interest and then accumulates counts over all individuals. Therefore, the person-occurrences measure confounds people and occurrences: using this measure, 1 occurrence for 10 people is counted the same as 10 occurrences for 1 person.

3.5 Selection of Urban Areas

The selection of urban areas to include in the exposure analysis takes into consideration the location of O_3 field and epidemiology studies, the availability of ambient O_3 data, and the desire to represent a range of geographic areas, population demographics, and O_3 climatology. These selection criteria are discussed further below in Section 4. Based on these criteria, staff plans to include the following 12 urban areas in the exposure analysis:

- Boston
- Philadelphia
- New York City
- Washington, D.C.
- Atlanta
- St. Louis
- Chicago
- Houston
- Los Angeles
- Detroit
- Cleveland.
- Sacramento

3.6 Exposure Periods

The exposure periods to be modeled will be the O_3-monitoring seasons for each urban area. These encompass the periods when high ambient O_3 levels are likely to occur, and are the periods for which routine hourly O_3 monitoring data are available. The O_3 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.

3.7 Populations to be Analyzed

Exposure modeling will be conducted for the general population residing in each area modeled, as well as for school-age children (ages 5 to 18), active school-age children, and asthmatic school-age children. 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 O_3-related health effects due to their increased dose rates. Levels of physical activity will be categorized by a daily Physical Activity Index (PAI), a measure of activity proportional to the metabolic equivalents of tasks (METS). METS is a unitless ratio of the energy expended performing an individual task to the person's basal metabolic rate. Children will be characterized as active if their median daily PAI over the period modeled is 1.75 or higher, a level characterized by exercise physiologists as being "moderately active" or "active" (McCurdy, 2000). Data from various national and state surveys undertaken by the Centers for Disease Control and Prevention (Kann, 2000) will be used to help assure the reasonableness of the proportions of children that are characterized as active. The proportion of the population of school-age children characterized as being asthmatic will be estimated by statistics on asthma prevalence rates.

3.8 Uncertainty and Variability

APEX is a Monte Carlo simulation model which explicitly incorporates the inherent variability of the model input data. Developing appropriate distributions representing variability and uncertainty in various model inputs (e.g., air exchange rates, O_3 decay rates, physiological parameters) is a key part of this modeling effort.

The primary difficulty in performing an uncertainty analysis is the quantitative characterization of the uncertainties of the model inputs and model formulation. We often have information about the variability of model inputs, and sometimes the variability and uncertainty combined, but it is usually difficult to estimate the uncertainty separately from the variability. However, for the APEX O_3 application, we have enough information to provide reasonable bounds or ranges for the uncertainties of many of the model inputs. We plan to assess the impacts of the uncertainties of the model inputs across these ranges, and use these results to inform a discussion of model uncertainties.

Staff plans to follow a 2-dimensional Monte Carlo/Latin hypercube sampling approach to a combined variability and uncertainty analysis for APEX. Essentially, a Monte Carlo approach entails performing many model runs with model inputs randomly sampled from specified distributions reflecting variability and uncertainty of the model inputs. The 2-dimensional Monte Carlo method allows for the separate characterization of the variability and uncertainty in the model results (Morgan and Henrion, 1990).

Due to the large number of APEX input parameters, it is unrealistic to perform a 2-dimensional Monte Carlo analysis of all of the inputs, due to the large number of model runs that would be required. We plan to first perform a 1-dimensional Monte Carlo uncertainty analysis of the model inputs to identify a limited number of input parameters that account for a major part of the uncertainty. A 2-dimensional analysis of variability and uncertainty would then be conducted, accounting for the uncertainty of these key inputs and the variability of all of the inputs.

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. In the absence of measurements that can be used to estimate model uncertainty, one must rely on informed judgment. Our 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 will discuss the simplifying assumptions and those uncertainties associated with the sub-models which are distinct from the input data uncertainties. Where possible, we will evaluate these sub-models by comparing their predictions with measured data. Otherwise, we will formulate an informed judgment as to a range of plausible uncertainties for the sub-models. We will quantitatively assemble the different types of uncertainties and variability to present an integrated analysis of uncertainty and variability.

The exposure analysis technical support document will provide a more detailed plan for uncertainty assessment. An analysis of variability will be described in the first draft of the O_3 Staff Paper; the uncertainty analysis will be presented in the second draft O_3 Staff Paper.

4 SCOPE AND APPROACH FOR HEALTH RISK ASSESSMENT

4.1 Overview

The health risk assessment will estimate various health effects associated with O_3 exposures for current O_3 levels, based on 2004 air quality data, as well as reductions in risk associated with attaining the current 8-h O_3 NAAQS and alternative O_3 standards, based on adjusting 2002-2004 air quality data. Risk estimates will be developed for 12 urban areas

located throughout the U.S. 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.

The methods used to conduct the risk assessment and summary results and key findings from the assessment will be presented in the first draft O_3 Staff Paper for current O_3 levels and for just meeting the current 8-h standard. The second draft O_3 Staff Paper will include risk estimates associated with just meeting alternative O_3 standards. In addition, a health risk assessment technical support document with a more detailed description of the methodology and results will accompany the O_3 Staff Paper.

4.2 Structure of the Risk Assessment

At this time, two general types of human studies are particularly relevant for deriving quantitative relationships between O_3 levels and human health effects: controlled human exposure studies and epidemiological and field studies. Controlled human exposure studies involve volunteer subjects who are exposed while engaged in different exercise regimens to specified levels of O_3 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 hyperresponsiveness, and inflammation. As noted above, prior EPA risk assessments for O_3 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 developed during the last review which was based on analysis of individual data that describes the relationship between a measure of personal exposure to O_3 and the measure(s) of lung function recorded in the study. The measure of personal exposure to ambient O_3 is typically some function of hourly exposures – e.g., 1-hour maximum or 8-hr maximum. Therefore, a risk assessment based on exposure-response relationships derived from controlled human exposure study data requires estimates of personal exposure to O_3, typically on a 1-hour or multi-hour basis. Because data on personal hourly O_3 exposures are not available, estimates of personal exposures to varying ambient concentrations are derived through exposure modeling, as described above in Section 3.

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 O_3 concentration is typically measured as the average of monitor-specific measurements, using population-oriented monitors. Population health responses for O_3 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, 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 should 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 location 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.

- 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 could not.

- 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 below.

4.3 Assessment of Risk Based on Controlled Human Exposure Studies

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 O_3 AQCD (EPA, 2005b), there are numerous controlled human exposure studies reporting lung function decrements (as measured by changes in FEV_1), 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).

4.3.1 Selection of health endpoints

In the last review, the health risk assessment estimated both lung function decrements ($\geq$10, $\geq$15, and $\geq$20% changes in FEV_1) and respiratory symptoms in children 6-18 years old associated with 1-hour exposures at moderate and heavy exertion and 8-hour exposures at moderate exertion. At that time EPA staff and the CASAC O_3 Panel judged that it was reasonable to estimate the exposure-response relationships for children 6-18 years old based on data from adult subjects (18-35 years old). As discussed in the 1996 O_3 Staff Paper (EPA, 1996a) and 1996 O_3 AQCD (EPA, 1996b), findings from other chamber studies (McDonnell et al., 1985) for children 8-11 year 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 O_3 under controlled chamber conditions. Staff intends to use the same approach in this assessment.

In the prior risk assessment, staff estimated risk for lung function decrements associated with 1-hour heavy exertion, 1-hour moderate exertion, and 8-hour moderate exertion exposures. Since the 8-hour moderate exertion exposure scenario clearly resulted in the greatest health risks in terms of lung function decrements, staff plans to include only the 8-hour moderate exertion exposures in the current risk assessment for this health endpoint.

Although respiratory symptoms in healthy children were estimated in the last review, staff does not plan to estimate respiratory symptoms in healthy children given the lack of symptoms found in field studies examining responses in children published since the prior review. While a number of controlled human exposure studies have been published since the last review reporting various other acute effects, including airway responsiveness and increases in inflammatory indicators, none of these studies were conducted at multiple concentration levels within the range of greatest interest (i.e., below 0.12 ppm). Thus, staff plans to limit this portion of the risk assessment to lung function decrements in children and to again base the exposure-response relationships on data obtained for 18-35 year old subjects.

4.3.2 Selection of exposure-response functions

Staff plans to use the same methodology used in the prior risk assessment (see Appendices A and B in Whitfield et al., 1996) to estimate probabilistic exposure-response relationships for lung function decrements associated with 8-h moderate exertion exposures. The combined data set from the Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991) studies are used to estimate exposure-response relationships for 8-h exposures. The data from these controlled human exposure studies are corrected for the effect of exercise in clean air to remove any systematic bias that might be present in the data attributable to an exercise effect. Generally, this correction for exercise in clean air is small relative to the total effects measures in

the O_3-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 O_3 concentrations.

4.3.3 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 active children experiencing 1 or more occurrences of a lung function decrement $\geq$ 15 and $\geq$ 20% in an O_3 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. The mean number of occurrences per child also will be calculated to provide an indicator of the average number of times that a responder would experience the specified effect during an O_3 season.

A headcount risk estimate for a given lung function decrement (e.g., $\geq$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 "as is" ambient O_3 concentrations, (2) estimate expected risk, given the personal exposures associated with estimated background ambient O_3 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:

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

where:

e_j = (the midpoint of) the jth category of personal exposure to ozone, given "as is" ambient O_3 concentrations;

e_i^b = (the midpoint of) the ith category of personal exposure to ozone, given background ambient O_3 concentrations;

P_j = the fraction of the population having personal exposures to O_3 concentration of e_j ppm, given "as is" ambient O_3 concentrations;

P_i^b = the fraction of the population having personal exposures to O_3 concentration of e_i^b ppm, given background ambient O_3 concentrations;

$RR_k \mid e_j$ = k-fractile response rate at O_3 concentration e_j;

$RR_k \mid e_i^b$ = k-fractile response rate at O_3 concentration e_i^b; and

N = number of intervals (categories) of O_3 personal exposure concentration, given "as is" ambient O_3 concentrations; and

N_b = number of intervals of O_3 personal exposure concentration, given background ambient O_3 concentrations.

For example, if the median expected response rate given "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 given 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.

4.3.4 Selection of urban areas

Staff plans to develop lung function decrement risk estimates for school age children and active school age children 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 O_3 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.

4.4 Assessment of Risk Based on Epidemiological and Field Studies

As discussed in the draft O_3 AQCD (EPA, 2005b), a significant number of epidemiological and field studies examining a variety of health effects associated with ambient O_3 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 O_3 risk assessment to include an assessment of selected health risks attributable to ambient O_3 concentrations over policy relevant background concentration and health risk reductions associated with attainment of current and alternative O_3 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 3. 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.

4.4.1 Selection of health endpoints

Staff has carefully reviewed the epidemiological evidence evaluated in Chapter 7 and summarized in Chapter 7 Annex of the draft O_3 AQCD (EPA, 2005b). Tables AX7-1 through AX7-5 summarize the available U.S. and Canadian studies of the effects of acute (short-term) exposures for various health effect categories. Given the substantial number of health endpoints and studies addressing O_3 effects, staff plans to include in this quantitative O_3 risk assessment only the better understood (in terms of health consequences) health endpoint categories for which the weight of the evidence supports the inference of a causal relationship between O_3 and the effect category. In addition, staff plans to include only those categories for which there are studies that satisfy the study selection criteria discussed below.

Based on its review of the evidence evaluated in the draft O_3 AQCD, staff is considering including in the epidemiology and field studies-based portion of the O_3 risk assessment the following broad categories of health endpoints associated with short-term exposures:

- respiratory symptoms in asthmatic children;
- school absences;
- emergency department visits for respiratory illness;
- hospital admissions for respiratory illness;
- unscheduled hospital admissions for respiratory illness; and
- premature total, respiratory, and cardiovascular mortality.

4.4.2. Selection of urban areas

Several objectives were considered in selecting potential urban areas for which to conduct the epidemiological studies-based O_3 risk assessment. Staff plans to include an urban area only if it satisfies the following criteria:

- It has sufficient air quality data for a recent year (2002 or later).
- It is the same as or close to the location where at least one concentration-response function for one of the recommended health endpoints (see above) has been estimated by a study that satisfies the study selection criteria (see below).
- For the hospital admission effects categories, relatively recent location-specific baseline incidence data, specific to International Classification of Disease (ICD) codes, are available.[4]

4 The absence of hospital admissions baseline incidence data does not necessarily mean that we cannot use an urban area in the risk assessment, only that we cannot use it for the hospital admissions endpoint.

Because baseline mortality incidence data are available at the county level, this is not a constraint in the selection of urban areas for the O_3 risk assessment. Information on the incidence of respiratory symptoms and illnesses not requiring hospitalization, in contrast, is generally not available, except in those locations in which studies were conducted. Data on hospital admissions for recent years, however, specific to ICD codes, are available in some cities but not others. This category of incidence data is therefore a consideration in the selection of urban areas to include in the analysis.

In addition, staff plans to take into account the following considerations in selecting from among those urban locations that satisfy the above selection criteria:

- Locations with more health endpoints are preferred over those with fewer.
- The overall set of urban locations should represent a range of geographic areas, population demographics, and O_3 climatology within the U.S..

Based on the selection criteria and additional considerations listed above, staff plans to include the following urban areas in our assessment of risk based on epidemiological and field studies:

- Boston
- Philadelphia
- New York City
- Washington, D.C.
- Atlanta
- St. Louis
- Chicago
- Houston
- Los Angeles
- Detroit
- Cleveland
- Sacramento

4.4.3 Selection of epidemiological and field studies

As discussed above, staff plans to include in the O_3 risk assessment only the better understood health effects for which the weight of the evidence supports a causal inference. Thus, in cases where none of the available studies reported a statistically significant relationship, the effect endpoint would not be included. Once it has been determined that a health endpoint will be included in the analysis, however, inclusion of a study on that health endpoint will not be based on statistical significance. That is, consistent with the approach being taken in the particulate matter (PM) risk assessment (see EPA, 2005c, Chapter 4, and Abt Associates, 2005), no credible study on an included health endpoint has been excluded from the analysis on the basis of lack of statistical significance.

Staff has applied the following selection criteria for any study that has estimated one or more O_3 concentration-response functions for a selected health endpoint in an urban location to be used for the O_3 risk assessment:

- It is a published, peer-reviewed study that has been evaluated in the draft O_3 AQCD (EPA, 2005b) and judged adequate by staff for purposes of inclusion in this risk assessment based on that evaluation.

- It directly measured, rather than estimated, O_3 on a reasonable proportion of the days in the study.

- It either did not rely on Generalized Additive Models (GAMs) using the S-Plus software to estimate concentration-response functions or has appropriately re-estimated these functions using revised methods.[5]

- For short-term mortality studies, that the study reported results for the O_3 season.

Staff notes that the draft O_3 AQCD is currently under review by the CASAC O_3 Panel and the general public. Accordingly, the final group of studies to be included in the planned risk assessment may change based on the advice and recommendations resulting from this review.

4.4.4 A summary of selected health endpoints, urban areas and studies

Based on applying the criteria and considerations discussed above, the health endpoints, urban locations, and epidemiology and field studies that staff plans to include in the O_3 risk assessment are given in Table 1. More detail on the studies is given in Table 2.

[5] The GAM S-Plus problem was discovered prior to the recent PM risk assessment that was carried out as part of the PM NAAQS review. It is discussed in the PM Criteria Document (EPA, 2004), second draft PM Staff Paper (EPA, 2005c), and draft PM Health Risk Assessment (Abt Associates, 2005).

Table 1. Locations and Health Endpoints Considered for Inclusion in the O_3 Risk Assessment Based on Epidemiological and Field Studies

Urban Area	Short-term Exposure Mortality	Respiratory Hospital Admissions	Emergency Room Visits for Respiratory Illness	School Absences	Respiratory Symptoms
Boston	Bell[A*]				
Philadelphia	Bell[A*] Huang[B**] Moolgavkar[N]				
New York	Bell[A*] Huang[B**]	Thurston[G]			
Washington, D.C.	Bell[A*]				Mortimer[L**]
Atlanta	Bell[A*] Huang[B**]		Tolbert[H] Friedman[I] Peel[J]		
St. Louis	Bell[A*]				Mortimer[L**]
Chicago	Bell[A]* Huang[B**] Schwartz[C*]				Mortimer[L**]
Houston	Bell[A*] Huang[B**] Schwartz[C*]				
Los Angeles	Bell[A*] Huang[B**]	Linn[F]		Gilliland[K]	
Sacramento	Bell[A*]				
Detroit	Bell[A*] Huang[B**] Schwartz[C*] Ito[D]				Mortimer[L**]
Cleveland	Bell[A*] Huang[B**]	Schwartz[E]	Jaffe[M]		Mortimer[L**]

* Study reports multi-city results based on a set of cities including city listed in this row. Single-city results have been obtained from the authors.

** Study reports multi-city results based on a set of cities including city listed in this row. Single-city results are also reported.

[A] Bell et al. (2004)
[B] Huang et al. (2004)
[C] Schwartz (2004)
[D] Ito (2003)
[E] Schwartz et al. (1996)
[F] Linn et al. (2000)
[G] Thurston et al. (1992)
[H] Tolbert et al. (2000)
[I] Friedman et al. (2001)
[J] Peel et al. (2005)
[K] Gilliland et al. (2001)
[L] Mortimer et al. (2002)
[M] Jaffe et al. (2003)
[N] Moolgavkar et al. (1995)

Table 2. Overview of Ozone Epidemiological and Field Studies Considered for Inclusion in the O_3 Health Risk Assessment

Study	Location(s)	Health Endpoint	Other Pollutants in Model	Analyses Limited to Ozone Season?	Statistically Significant Effects?
Mortality					
Bell et al., 2004	multi-city function based on 95 cities	total (non-injury) mortality cardiovascular and respiratory mortality	No*	Yes	Yes
Huang et al., 2004	19 U.S. cities multi-city with single city and multi-city estimates	cardiovascular and respiratory mortality	CO, SO2, NO2, PM10 - each in a separate 2-pollutant model with O3	Yes (summer only)	Yes - for single-pollutant model Mixed - for 2-pollutant models
Moolgavkar et al., 1995	Philadelphia	total non-accidental mortality	TSP, SO2	Yes	Yes – for summer
Schwartz, 2004	14 U.S. cities	total non-accidental mortality	PM10	Yes	Yes– for full yr and warm season, but not cold season
Ito, 2003	Detroit, MI	Total, circulatory, and respiratory mortality	PM10	Yes	Yes
Hospital admissions					
Linn, et al. 2000	Los Angeles, CA	Hospital admissions for pulmonary illness among people age 30+	No	Yes	No
			PM10, CO, NO2	Yes	No
Schwartz et al, 1996	Cleveland, OH	Hospital admission for resp. illness among people age 65+	No	Yes	Yes
Thurston et al., 1992	New York City, NY	unscheduled hospital admission for respiratory illness	No	Yes (summers only)	Yes

Study	Location(s)	Health Endpoint	Other Pollutants in Model	Analyses Limited to Ozone Season?	Statistically Significant Effects?
Emergency room visits for:					
Friedman, et al. 2001	Atlanta, GA	"acute care events" for asthma among children ages 1 - 16***	No	Yes (June 21 - Sept. 1)	Yes - for 2-day and 3-day cumulative exposures for some databases***
Jaffe et al., 2003	Cleveland, OH Cleveland, Cincinnati, and Columbus combined	Asthma, among people ages 5-34	No	Yes (June – August)	No
Peel et al. 2005	Atlanta, GA	all respiratory illnesses	Yes******	Yes	Yes
		Asthma	Yes******		No
		Pneumonia	Yes******		No
		COPD	Yes******		No
		URI	Yes		Yes
Tolbert et al. 2000	Atlanta, GA	Pediatric ER visits for asthma	No	Yes (summer only)	Yes
School absenteeism					
Gilliland, et al. 2001	Los Angeles, CA	due to all illness; resp. illness; upper resp. illness; lower resp. illness, among 4th grade children.	No	No (January-June)	Yes for all categories
Respiratory symptoms					
Gent et al. 2003****	CT and Springfield, MA	respiratory symptoms in asthmatic children under 12 (at time of enrollment in study)	No	Yes (April-September)	Yes - for some symptoms, among medicated users only

Study	Location(s)	Health Endpoint	Other Pollutants in Model	Analyses Limited to Ozone Season?	Statistically Significant Effects?
Mortimer, et al. 2002	multi-city (8 locations in U.S.)	Morning asthma symptoms in asthmatic children 4 – 9 years old	PM10, SO2, NO2	Yes (June-August)	Yes - for single-pollutant model only

* The authors report that the results were robust to adjustment for PM_{10}, but do not report the multi-pollutant functions.

** This study was carried out using GAM S-Plus before the GAM S-Plus problem was realized. The data were reanalyzed as part of the general HEI-sponsored reanalysis of studies that used GAM S-Plus (see Ito 2003), but with an emphasis on PM. Reanalyzed results for O_3 are presented graphically in the publication but numerical results have been obtained from the author.

***All results are given separately for the 4 separate data sources – Georgia Medicaid claims file; Health maintenance organization; Pediatric emergency departments, and Georgia Hospital Discharge Database. The types of asthma events covered by the sources are: emergency care and hospitalizations; emergency care, urgent care, and hospitalizations; emergency care and hospitalizations; and hospitalizations, respectively.

****Asthmatic children were divided into 2 groups: those who use maintenance medication and those who do not. This study can be used only if we are able to obtain information about the proportion of asthmatic children who use maintenance medication.

*****All exposures were lagged 3 days.

******Authors conducted multi-pollutant analyses but did not present quantitative results in publication for this health endpoint.

4.4.5 Selection of concentration-response functions

Studies often report more than one estimated concentration-response function for the same location and health endpoint. Sometimes models including different sets of co-pollutants are estimated in a study; sometimes different lags are estimated. In some cases, two or more different studies estimated a concentration-response function for O_3 and the same health endpoint in the same location (this is the case, for example, with O_3 and mortality associated with short-term exposures). For some health endpoints, there are studies that estimated multi-city O_3 concentration-response functions, while other studies estimated single-city functions.

All else being equal, staff judges that a concentration-response function estimated in the assessment location is preferable to a function estimated elsewhere, since it avoids uncertainties related to potential differences due to geographic location. That is why the urban areas selected for the epidemiological studies-based O_3 risk assessment are those locations in which concentration-response functions have been estimated. 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. When they are estimating a single concentration-response function based on several cities, 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 coefficient. Because single-city and multi-city studies have different advantages, if a single-city concentration-response function has been estimated in a risk assessment location and a multi-city study which includes that location is also available for the same health endpoint, staff plans to use both functions for that location in the risk assessment.

Several O_3 epidemiological studies estimated concentration-response functions in which O_3 was the only pollutant entered into the health effects model (i.e., single pollutant models) as well as other concentration-response functions in which O_3 and one or more co-pollutants (e.g., PM, nitrogen dioxide, sulfur dioxide, carbon monoxide) were entered into the health effects model (i.e., multi-pollutant models). To the extent that any of the co-pollutants present in the ambient air may have contributed to the health effects attributed to O_3 in single pollutant models, risks attributed to O_3 might be overestimated where concentration-response functions are based on single pollutant models. However, if co-pollutants are highly correlated with O_3, their inclusion in an O_3 health effects model can lead to misleading conclusions in identifying a specific causal pollutant. When collinearity exists, inclusion of multiple pollutants in models often produces unstable and statistically insignificant effect estimates for both O_3 and the co-pollutants. Given that single and multi-pollutant models each have both potential advantages and disadvantages, with neither type clearly preferable over the other in all cases, staff plan to report risk estimates based on both single and multi-pollutant models where both are available.

Epidemiological and field studies often present several concentration-response functions, each incorporating a different lag structure. The question of lags and the problems of correctly specifying the lag structure in a model have been discussed extensively [see, for example, the

PM AQCD (EPA, 2004, section 8.4.4); the second draft PM Staff Paper (EPA, 2005c, sections 3.5.5.2 and 4.2.6.3); the draft O_3 AQCD (EPA, 2005b, section 7.1.3.3); and Schwartz, 2000). The draft O_3 AQCD notes that "simply choosing the most significant exposure lag may bias the air pollution risk estimates away from the null ..." (EPA, 2005b, section 7.1.3.3). On the other hand, there is recent evidence (Schwartz, 2000) that the relationship between PM and health effects may best be described by a distributed lag (i.e., the incidence of the health effect on day n is influenced by PM concentrations on day n, day n-1, day n-2 and so on). If this is true for O_3 as well, then a model with only a single lag may bias air pollution risk estimates towards the null. For mortality associated with short-term exposure to O_3, Huang et al. (2004) present the results for a distributed lag model that takes into account exposure from the previous 6 days. When a study reports several single lag models for a health effect, staff plans to base our initial selection of the appropriate lag structure for each health effect on the overall assessment provided in the draft O_3 AQCD, based on all studies reporting concentration-response functions for that health effect.

In summary:

- if a single-city concentration-response function has been estimated in a risk assessment location and a multi-city study which includes that location is also available for the same health endpoint, staff plans to use both functions for that location in the risk assessment;

- risk estimates based on both single and multi-pollutant models will be used where both are available;

- where available, distributed lag models will be used; when a study reports several single lag models for a health effect, staff plans to base our initial selection of the appropriate lag structure for the health effect on the overall assessment in the draft O_3 AQCD, based on all studies reporting concentration-response functions for that health effect.

4.4.6 Baseline health effects incidence considerations

The most common epidemiologically-based health risk model expresses the reduction in health risk (Δy) associated with a given reduction in O_3 concentrations (Δx) as a percentage of the baseline incidence (y). To accurately assess the impact of O_3 air quality on health risk in the selected urban areas, information on the baseline incidence of health effects (i.e., the incidence under "as is" air quality conditions) in each location is therefore needed. Where at all possible, staff plans to use county-specific incidences or incidence rates (in combination with county-specific populations). Estimates of location-specific baseline mortality rates can be obtained for each of the O_3 risk assessment locations for 2001 from CDC Wonder, an interface for public health data dissemination from the Centers for Disease Control (CDC).[6]

Hospital admissions studies being considered for inclusion in the O_3 risk assessment were conducted in Los Angeles, New York City, and Cleveland. ICD code-specific baseline hospital

[6] See http://wonder.cdc.gov/.

admission rates for Los Angeles County can be obtained from California's Office of Statewide Health Planning and Development, which provided records of hospital admissions for the study by Linn et al. (2000). The records provided for the Linn study included both ICD codes and All-Patient-Refined Diagnosis-Related Group (APR-DRG). Because Linn et al. (2000) used diagnosis categories based on the APR-DRG, staff will ensure that information obtained from California's Office of Statewide Health Planning and Development also contains the APR-DRG so that the baseline incidence rates are calculated for hospital admissions categories that match those used in the Linn study.

Schwartz et al. (1996) report several percentiles as well as the mean of the distribution of daily hospital admissions for respiratory illness (ICD-9 codes 460-519) in Cleveland, Ohio during the years 1988-90 (although the source of the information is not given). Staff plans to investigate the possibility of updating these baseline incidence rates.

Thurston et al. (1992) report 1990 population, as well as average unscheduled hospital admissions per day for respiratory illnesses and for asthma separately, for 1988 and for 1989 in New York City (and other cities in New York State), based on data on unscheduled (emergency) hospital admissions collected by the Statewide Planning and Research Cooperative System (SPARCS), a division of the New York State Department of Health. Baseline incidence rates for 1989/90 can be calculated using the data presented by Thurston et al. (1992). Alternatively, staff also plans to investigate the possibility of obtaining more recent data on unscheduled hospital admissions for respiratory illness and asthma in New York City from SPARCS with which to calculate more recent baseline incidence rates.

Tolbert et al. (2000) and Peel et al. (2005) report average daily emergency department visits for the relevant health effects in the facilities participating in their studies in the Atlanta area, which, in both studies, are reported to cover about 80 percent of the relevant emergency department visits. Staff plans to use either the average daily rates reported in the studies, in which case the baseline incidence will be understated; or alternatively, to adjust the baseline incidence upward, based on the authors' assessment that the facilities included in their studies cover about 80 percent of emergency room visits. It is less clear at this time whether baseline incidence can be constructed or obtained for the study by Friedman et al. (2001), which considers "acute asthma events" separately in five databases (see Table 2).

For other morbidity endpoints, such as respiratory symptoms in children, incidence information aggregated at higher than the city- or county-level may be all that is available. Staff plans to use the level of aggregation closest to county-specific; however, for some morbidity endpoints, it may be necessary to estimate county-specific incidence using national-level incidence rates. For some health endpoints, there may be no information on incidence other than the information provided for the city or county in which the concentration-response function was estimated. The rationale for the choice of incidence data used for each health endpoint in each location will be presented in the risk assessment technical support document.

Lack of location-specific incidence data will increase the uncertainty surrounding estimates of risk for the specific cities selected for the risk assessment. To the extent possible,

staff plans to provide a quantitative comparison to help assess the accuracy of using incidence rates at a higher level of aggregation (e.g., national incidence rates) by comparing these rates to county-specific incidence rates where these are available.

4.4.7 Assessing risk in excess of policy-relevant background

As noted above, staff plans to assess risks associated with O_3 concentrations in excess of policy-relevant background concentrations, and to assess risk reductions associated with just meeting current and alternative O_3 standards. Following the methods used in the prior O_3 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 O_3 concentrations in excess of policy-relevant background concentrations, staff will first calculate the difference between "as is" O_3 levels and policy-relevant background. Staff will then calculate the corresponding change in incidence of the health effect associated with that change in ambient O_3 concentration. If Δx denotes the change in O_3 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

$$\Delta y = y * [e^{\beta * \Delta x} - 1] \qquad \text{(Equation 4-2)}$$

where y denotes the baseline incidence (discussed above in Section 4.4.6) and β is the coefficient of O_3 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" O_3 levels and the O_3 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 O_3 levels that will be estimated to exist if the current standards are just met and O_3 levels that will be estimated to exist if the alternative, more stringent, standards are just met.

Because the O_3 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 O_3 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), following the method used in the draft PM risk assessment (Abt Associates, 2005).

4.5 Uncertainty and Variability

There are several uncertainties that affect the inputs to both the controlled studies-based and epidemiology-studies based portion of the O_3 risk assessment. These include uncertainties in the air quality adjustment procedures used to simulate attainment of standards, policy-relevant background estimates, exposure estimates, baseline incidence rates, and appropriate model form for the concentration- and exposure-response relationships used in the risk assessment. There also is likely city-to-city variability in both exposure estimates, discussed previously in section 3.71, and in concentration-response and exposure-response relationships.

For the portion of the risk assessment based on exposure-response functions derived from controlled human exposure studies, risk estimates will be prepared that incorporate the characterization of uncertainty and variability in the exposure estimates discussed previously in section 3.7.1. In addition, for the exposure-response relationships derived from the controlled human exposure studies the uncertainties due to sample size considerations also will be included in these risk estimates. Additional uncertainties for the controlled human exposure studies portion of the risk assessment will be discussed qualitatively and the most important ones will be addressed in sensitivity analyses described below.

With respect to the epidemiology-based portion of the risk assessment, the uncertainty that arises due to sample size considerations, that is reflected in the confidence intervals for the concentration-response relationships reported in the epidemiology studies, will be incorporated in this portion of the risk assessment. In the case of short-term exposure mortality, two studies, Bell et al. (2004) and Huang et al. (2004), provide both city-specific and overall multi-city mean estimates. In a prior risk assessment for PM, EPA used an Empirical Bayes technique to adjust location-specific estimates and their standard errors (Post et al., 2001). This approach effectively moves the city-specific estimates towards the overall mean; the larger the city-specific standard error (relative to the inter-city variability), the more the city-specific estimate is moved towards the overall mean of the distribution. This adjustment more efficiently uses the information in the study to yield estimates of the O_3 coefficient in each location and, thus better addresses concerns about city-to-city variability. The Bell et al. (2004) city-specific estimates already reflect this type of approach. Staff plans to use a similar approach to incorporate the Huang et al. (2004) concentration-response coefficients, which are for a distributed lag model, in this O_3 risk assessment.

Staff also notes that several meta-analyses addressing the impact of various factors on estimates of mortality associated with short-term exposures to O_3 have recently been accepted for publication and will be published in June 2005. Staff plans to review these analyses and explore whether they provide additional information that can be used to assist in characterizing the uncertainties associated with risk estimates for this health outcome.

For other sources of uncertainty in both the controlled human exposure-based and epidemiology-based portions of the risk assessment (e.g., the use of alternative model forms for the C-R function), there is insufficient information to incorporate these uncertainties probabilistically into the risk assessment. Staff plans to include sensitivity analyses, briefly

described in Table 3 below, to help characterize how important these uncertainties are to the risk estimates. These sensitivity analyses are designed to show the impact of changing the values of the most important uncertain inputs or assumptions underlying the analysis on the results of the O_3 risk assessment. The air quality-related uncertainties impact both the controlled human exposure and epidemiology-based portions of the risk assessment. The uncertainty about exposure-response relationships affects the controlled human exposure based portion of the assessment. Uncertainties about baseline incidence and concentration-response relationships derived from epidemiology studies impacts the epidemiology-based portion of the risk assessment.

Table 3. Planned Sensitivity Analyses

Component of the Risk Assessment	Sensitivity Analysis
Air Quality	A sensitivity analysis of the effect of different assumptions about background O_3 levels on estimated risks associated with "as is" levels of O_3 above background levels
Air Quality	A sensitivity analysis of the effect of different air quality adjustment procedures on the estimated risk reductions resulting from just meeting the current 8-h standard and alternative standards
Exposure-Response	A sensitivity analysis of the effects of alternative extrapolations of exposure-response models (below the lowest exposure levels used in the laboratory studies), including possible alternative hypothetical thresholds, on the estimated lung function risks (e.g., percentages of people experiencing lung function decrements of at least 10%, 20%, etc.) associated with "as is" levels of O_3 above background levels and risk reductions associated with just meeting alternative standards
Baseline Incidence	A comparison of using more aggregate baseline incidence data (national, state, etc) versus county-specific information in the county with the best local baseline incidence data
Concentration-Response	A sensitivity analysis of the effects of alternative hypothetical thresholds on estimated risks associated with "as is" levels of O_3 above background levels and risk reductions associated with just meeting alternative standards

5 SCHEDULE AND MILESTONES

Table 4 below includes the key milestones for the exposure analysis and health risk assessment that will be conducted as part of the current O_3 NAAQS review. A consultation with the CASAC O_3 Panel is planned for May 5, 2005 to obtain input on this draft Scope and Methods Plan. Staff will then proceed to develop exposure and health risk estimates associated with recent O_3 levels and levels adjusted to just meet the current 8-hour O_3 standard. These estimates and the methodology used to develop them will be discussed in the first draft O_3 Staff Paper and in separate exposure analysis and risk assessment technical support documents. These draft reports will be released for CASAC and public review in conjunction with the release of the first draft O_3 Staff Paper by the end of September 2005. EPA will receive comments on these draft documents from the CASAC O_3 Panel and general public at a meeting in December 2005. As noted earlier in section 3.7.1, staff anticipates including a fuller treatment of uncertainty and variability in the revised exposure analysis and health risk assessment that will be prepared following the December 2005 CASAC review meeting. The revised exposure analysis and risk assessment reports will also include estimates associated with just meeting any alternative standards that may be recommended by staff for consideration. The revised analyses will be released in April 2006 in conjunction with a second draft O_3 Staff Paper for review by CASAC and public at a meeting to be held in July 2006. Staff will consider these review comments and prepare final exposure analysis and risk assessment reports by September 2006.

Table 4. Key Milestones for the Exposure Analysis and Health Risk Assessment for the O_3 NAAQS review

Milestone	Date
Release 1st draft O_3 AQCD	January 31, 2005
Release draft Scope and Methods Plan	April 2005
CASAC/public review and meeting on 1st draft O_3 AQCD	May 4-5, 2005
CASAC consultation on draft Scope and Methods Plan	May 5, 2005
Release 2nd draft O_3 AQCD	August/September 2005
Release 1st drafts of the O_3 Staff Paper and the Exposure Analysis and Risk Assessment reports	September 2005
CASAC/public review and meeting on 2nd draft O_3 AQCD and 1st drafts of the O_3 Staff Paper and the Exposure Analysis and Risk Assessment reports	December 2005
Final O_3 AQCD	February 28, 2006
Release 2nd drafts of the O_3 Staff Paper and the Exposure Analysis and Risk Assessment reports	April 2006
CASAC/public review and meeting on 2nd drafts of the O_3 Staff Paper and the Exposure Analysis and Risk Assessment reports	July 2006
Final O_3 Staff Paper, Exposure Analysis, and Risk Assessment	September 2006

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Figure 1. Overview of the APEX Model

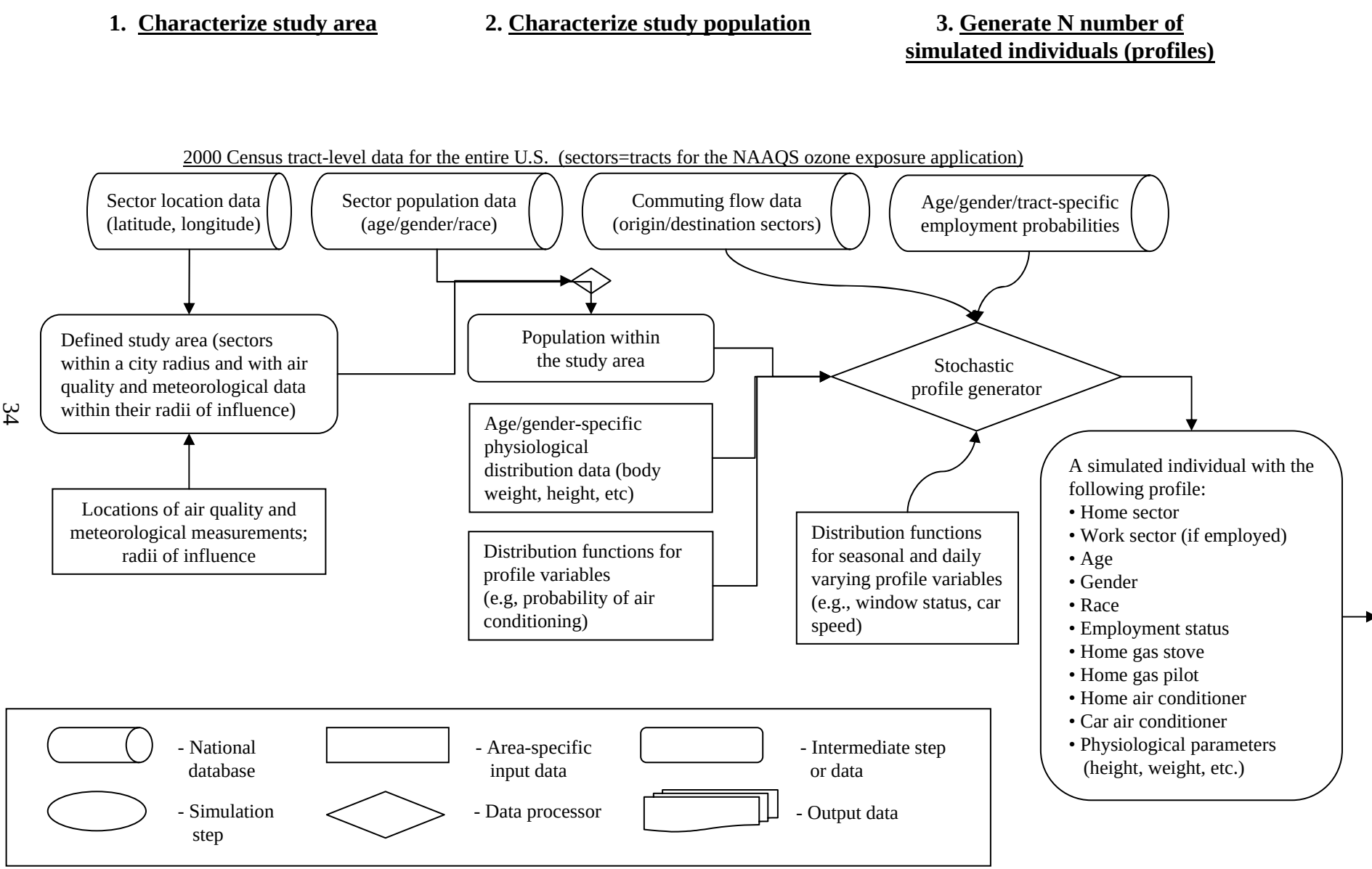
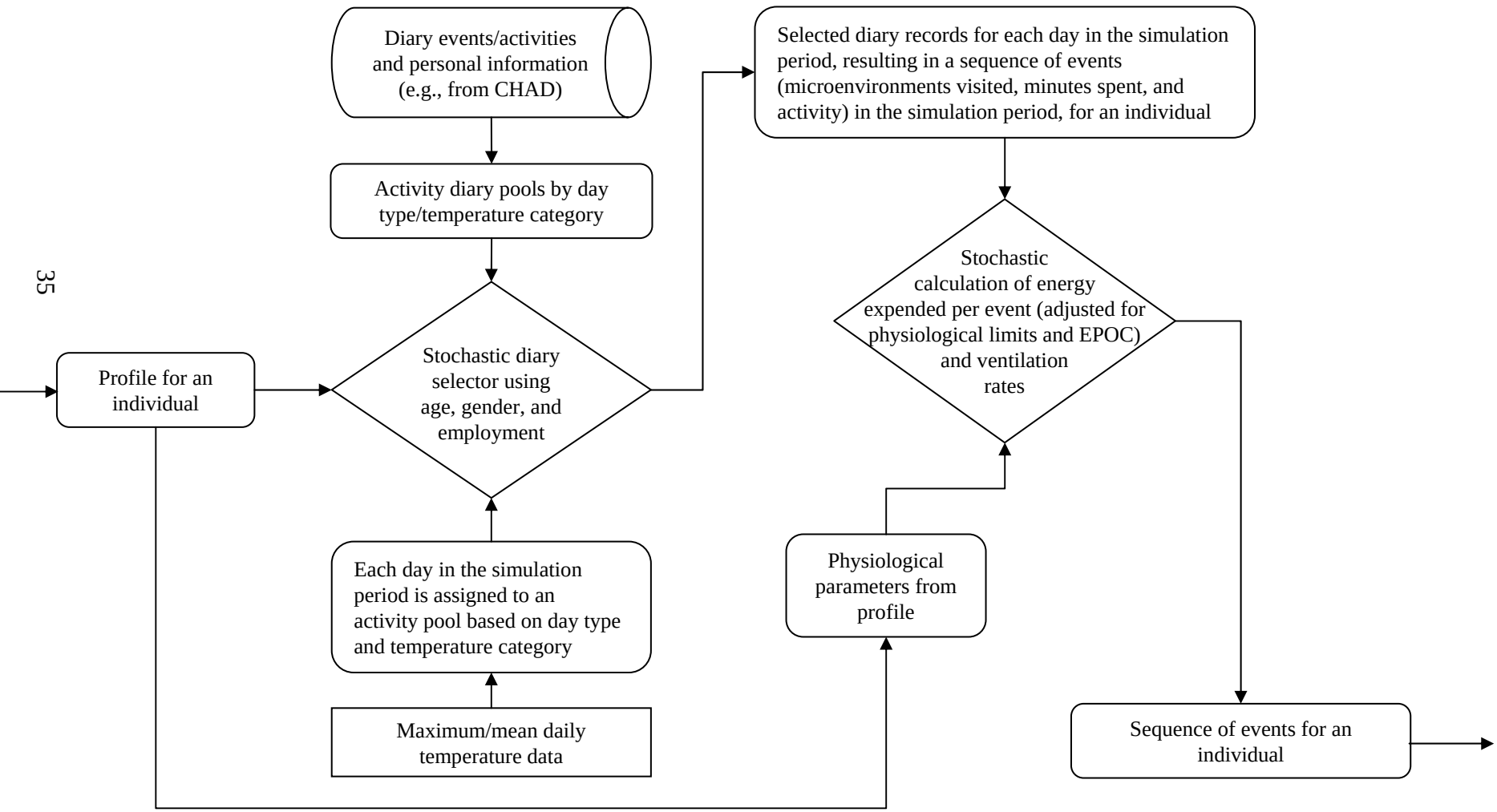


Figure 1. Overview of the APEX Model, continued



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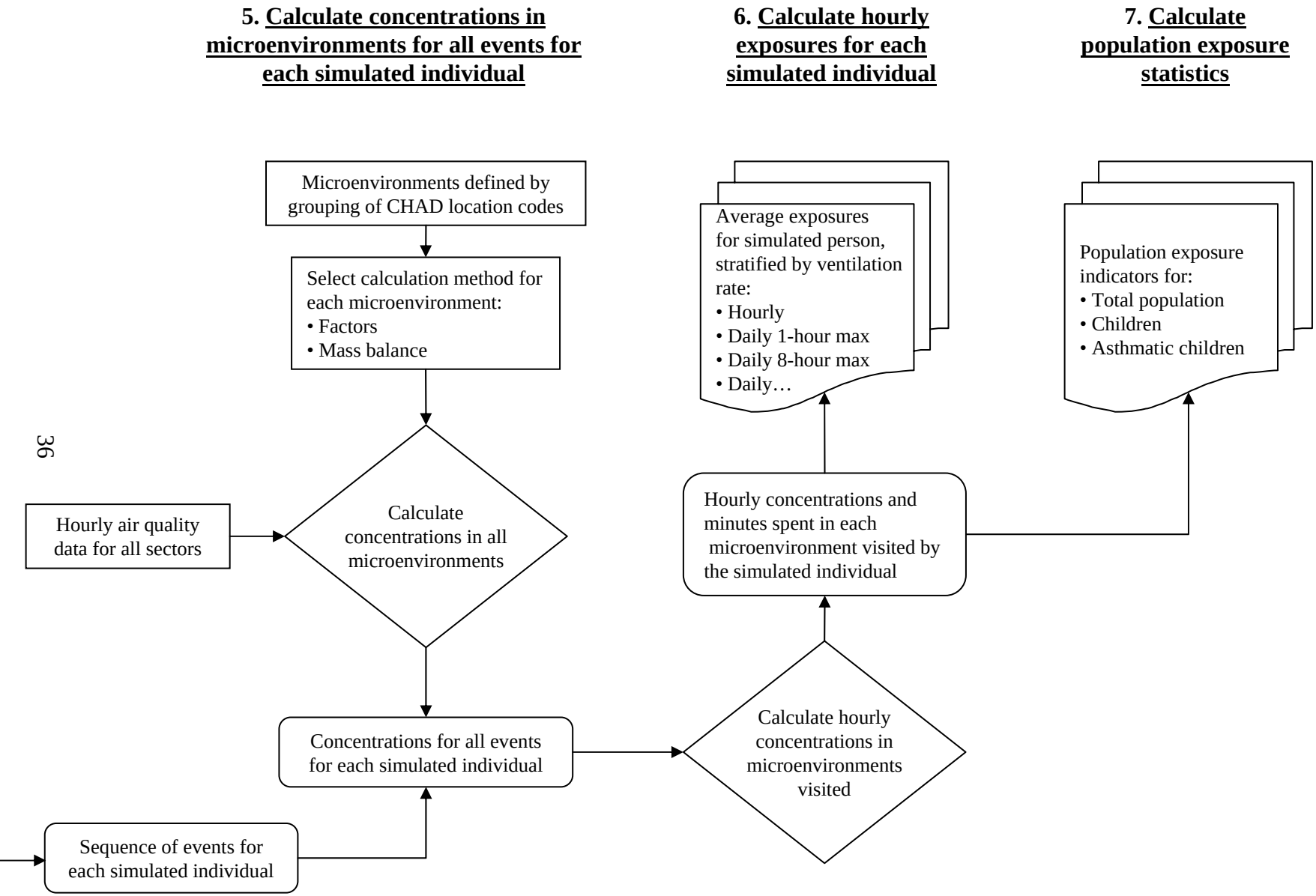

Figure 2. Major Components of Ozone Health Risk Assessment Based on Controlled Human Exposure Studies

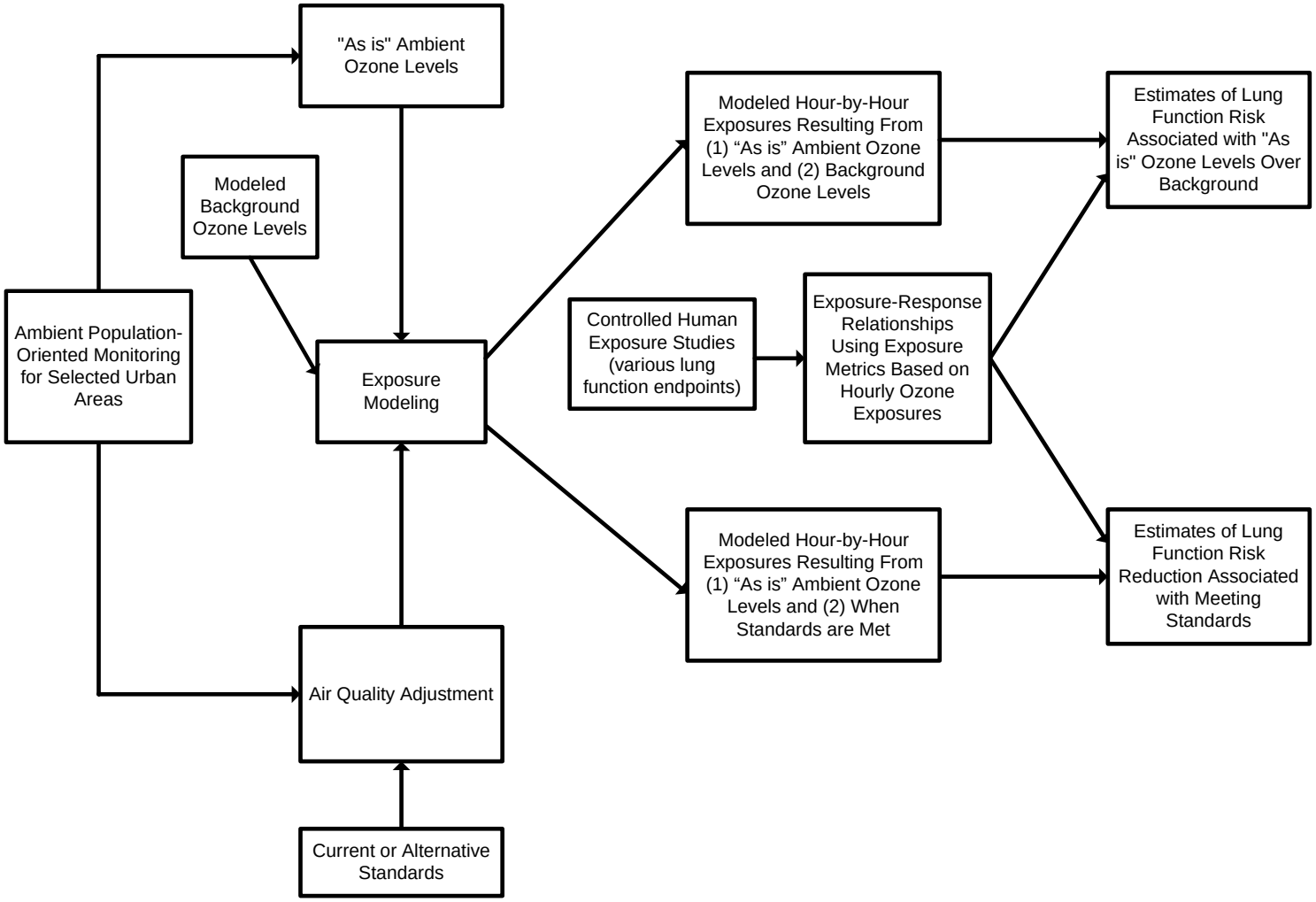

Figure 3. Major Components of Ozone Health Risk Assessment Based on Epidemiology and Field Studies