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Nitrogen Dioxide Health Assessment Plan: Scope and Methods for Exposure and Risk Assessment

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DISCLAIMER

This draft scope and methods plan has been prepared by staff from the Ambient Standards Group, Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency. Any opinions, findings, conclusions, or recommendations are those of the authors and do not necessarily reflect the views of the EPA. This document is being circulated to obtain review and comment from the Clean Air Scientific Advisory Committee (CASAC) and the general public. Comments on this document should be addressed to Dr. Stephen E. Graham, U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, C504-06, Research Triangle Park, North Carolina 27711 (email: graham.stephen@epa.gov).

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1. INTRODUCTION

The U.S. Environmental Protection Agency (EPA) is presently conducting a review of the national ambient air quality standards (NAAQS) for nitrogen dioxide (NO_2). 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 plan and schedule for this NO_2 NAAQS review is presented in the *Plan for Review of the Primary National Ambient Air Quality Standard for Nitrogen Dioxide* (US EPA, 2007a). That plan discusses the preparation of two key components in the NAAQS review process: an Integrated Science Assessment (ISA) and risk/exposure assessments. The ISA (US EPA, 2007b) critically evaluates and integrates scientific information on the health effects associated with exposure to oxides of nitrogen (NO_x) in the ambient air. The risk/exposure assessments will develop, as appropriate, quantitative estimates of human exposure and health risk and related variability and uncertainties, drawing upon the information summarized in the ISA. This draft document describes the scope and methods planned for the conduct of these assessments.

1.1 OVERVIEW 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 NO_2 under existing air quality levels, upon just meeting the current NO_2 primary NAAQS, and upon just meeting potential alternative standards that may be under consideration. The risk/exposure assessments will draw upon the information presented in the Integrated Science Assessment (ISA) and related Annexes. This includes information on atmospheric chemistry, air quality, human exposure, the impact of local source emissions, and health effects of concern. Nitrogen dioxide is one of a group of substances known as nitrogen oxides (NO_x), which include multiple gaseous (e.g., NO_2, NO) and particulate (e.g., nitrate) species. As in past NAAQS reviews, NO_2 will be considered as the

[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."

surrogate for the gaseous NO_x species for the purpose of this assessment, with particulate species addressed as part of the particulate matter (PM) NAAQS review.

The planned NO_2 exposure and health risk assessments are designed to estimate short-term and long-term exposures to NO_2 and associated health effects. Risks and exposures will be assessed using a tiered approach where progression to a more sophisticated level of analysis will depend on the availability of data and on the anticipated utility of the results. For example, exposure will be assessed through the use of ambient air quality as a surrogate for exposure or by supplementing the existing ambient monitoring data with local source concentration measures and/or model estimates, where appropriate. In addition, the exposure estimates may involve incorporating human activity data and microenvironmental concentrations or possibly the development of individual exposure profiles. The particular form of the exposure assessment selected would generate ambient concentrations as well as exposure metrics that are consistent with the available information on health effects associated with NO_2 exposure.

Health risk will initially be assessed through the identification of concentration levels associated with adverse health effects, termed *potential health effect benchmarks*. These potential health effect benchmarks, obtained from clinical health studies and evaluated in the ISA, will then be used to determine how often air quality concentrations or estimated exposures exceed concentrations associated with adverse health effects. In general, the exposure estimates generated will serve as a measure of comparison to identified potential health effect benchmarks to 1) estimate the number of individuals experiencing exposures of concern, and 2) estimate the range of exposures above levels of concern. Most of the recent supporting evidence for NO_2 health effects however is from epidemiological studies, resulting in uncertainties regarding whether the variation in observed health effects are caused by ambient NO_2 or perhaps by exposure to one or more correlated chemicals. An additional characterization of risk may involve use of concentration-response functions, if and where sufficient and relevant data are identified in the ISA to support development of such functions and related to ambient NO_2 concentrations.

This plan is intended to facilitate consultation with the CASAC, as well as for public review, and to obtain advice on the overall scope, approaches, and key issues in advance of the conduct of such analyses and presentation of results in the first draft of the risk/exposure assessments. The risk/exposure assessments together with other information contained in the NO_x ISA, are intended to help inform the Administrator's judgments as to 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 ON NO_2 NAAQS

As a first step in formulating the scope and methods plan, a point of reference was developed by extracting key supporting results from the previous review of the NAAQS for NO_2 (US EPA, 1995). In the previous NO_2 NAAQS review, exposure was assessed using ambient monitoring data as a surrogate for exposure. That assessment primarily targeted long-term air quality trends as indicated by analysis of ambient monitoring data (US EPA, 1995). Taking the previous assessment into consideration, the annual standard of 0.053 ppm was retained to protect against long-term exposures and resultant health effects. However, the variability in ambient concentrations and the potential for exposure to short-term peak concentrations was also considered.

At the time of the previous standard review, a few studies indicated the possibility of adverse health effects due to short-term exposures of about 0.20 ppm averaged across a 1-hour time period. As a result, the frequency of ambient concentrations in excess of 0.15 ppm to 0.30 ppm (1-hr average) was estimated (McCurdy, 1994). Two analyses were performed; one considered ambient monitoring data from the Los Angeles Consolidated Metropolitan Statistical Area (CMSA) and the other included CMSA monitoring sites across the rest of the U.S., excluding the Los Angeles CMSA. These analyses used ambient monitoring data from the years 1988-1992 and screened for sites with at least one hourly exceedance of selected short-term health effect benchmarks in a year. Of the 107 monitoring values obtained using this criteria (a total of 31 were within the Los Angeles CMSA), 4 had annual average concentrations greater than the annual standard of 0.053 ppm, all of which were in the Los Angeles CMSA. Predictive models were constructed that related the frequency of hourly concentrations above potential short-term health effect benchmarks to a range of annual average concentrations, including the current standard. Based on the results of this analysis, both CASAC (Wolff, 1995) and the Administrator (60 FR 52874) concluded that the minimal occurrence of short-term peak concentrations at or above a potential health effect benchmark of 0.20 ppm (1-hr average) indicated that the current annual standard would provide adequate health protection against short-term exposures.

The planned exposure analysis and health risk assessment described in this Scope and Methods Plan builds upon the methodology, analyses, and lessons learned from the assessments conducted for the last review. These plans are based on our current understanding of the NO_2 scientific literature and are subject to change as findings of the first draft NO_2 ISA are reviewed by the CASAC and general public. Currently, EPA's Office of Research and Development (ORD) National Center for Environmental Assessment (NCEA) has compiled and synthesized the most policy-relevant science available to produce a first draft of the ISA (US EPA, 2007b), portions of which have been reviewed and used in the development of the approach below. The approach described in this plan may also be modified according to CASAC and public comments following their review of this document as well as be guided by any additional information contained in the second and final versions of the ISA.

2. AIR QUALITY CONSIDERATIONS

The latest years of NO_2 air quality data available since the previous review (1995-2006) have been assembled for use in the exposure and health risk analyses, where use of particular years of data is determined to be appropriate. The following air quality scenarios will be considered:

- "*as is*" representing the historical and recent ambient monitoring hourly concentration data as reported by US EPA's Air Quality System (AQS).
- "*simulated*" concentrations are those that have been modified by a mathematical or statistical procedure to just meet a particular concentration level for a specific averaging time representing the current and/or alternative NO_2 NAAQS. Simulations of this type would use the most recent ambient monitoring data (years 2004-2006).

Various approaches to performing such simulations are being considered, including both linear and non-linear procedures. Currently, every location across the U.S. meets the current NO_2 annual standard (Figure 1) (US EPA, 2007d), thus the simulation of air quality data would be useful in evaluating just meeting alternative standards that are more stringent than the current standard (often referred to as a concentration roll-back). Typically, ambient concentrations are not adjusted higher to simulate just meeting alternative standards, therefore older historical data may be of use in representing scenarios that are at or near the current NO_2 standard.

Another air quality issue to be addressed includes the characterization of policy-relevant background (PRB) levels in the U.S, which is defined as the distribution of NO_2 concentrations that would be observed in the U.S. in the absence of anthropogenic (man-made) emissions of NO_2 precursors in the U.S., Canada, and Mexico. Estimates of PRB have been reported in the draft ISA (Section 5.5) and Annexes (AX2.9), and for most of the continental U.S. the PRB is estimated to be less than 300 parts per trillion (ppt). In the Northeastern U.S. where present-day NO_2 concentrations are highest, this amounts to a contribution of about 1% percent of the total observed ambient NO_2 concentration (AX2.9). Since it is well below concentrations that might be considered to cause a potential health effect, it will not be used separately in any estimation of health risk. In addition, this low contribution would provide support for a proportional method to adjust air quality, i.e., an equal adjustment of air quality values across the entire air quality distribution to just meet a target value.

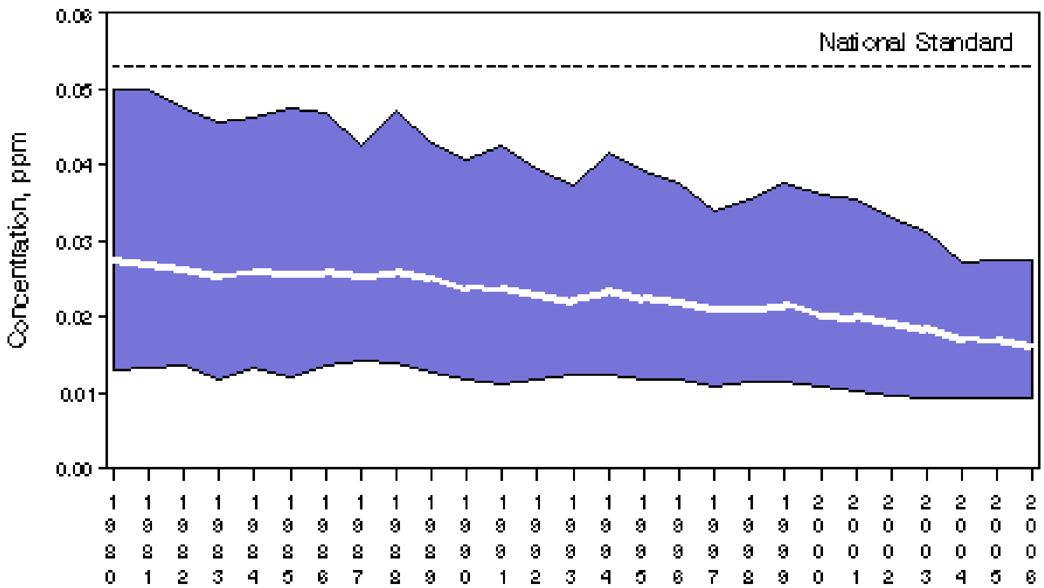

Figure 1. Monitoring Site Annual Average NO_2 Ambient Concentrations Between 1980 and 2006 (white line) Based on 87 Active Sites. Upper and Lower Shaded Areas Include Those Sites with Concentrations Below the 90th Percentile and Above the 10th Percentile Concentrations, Respectively.

3. EXPOSURE ASSESSMENT SCOPE AND METHODS

3.1 OVERVIEW

The exposure assessment for NO_2 will estimate human exposures associated with current ambient levels of NO_2, with ambient levels that just meet the current standard, and with ambient levels that just meet alternative standards that may be under consideration. A three-tiered approach to assessing exposure will be employed, beginning with an air quality characterization and progressing to a more refined analysis, if appropriate. The goals of the NO_2 exposure assessment are: (1) to estimate short- and long-term exposures to ambient concentrations through air quality monitoring and modeling analyses that consider current air quality for NO_2 and air quality levels just meeting the current and potential alternative NO_2 standards; (2) to develop quantitative relationships between long-term average and short-term peak concentrations; and (3) to identify key assumptions and uncertainties in the exposure estimates. The results from the air quality analysis and exposure assessment would be used to inform the characterization of population risks, as described in Section 4.

Several tools would be used to assess exposure within the specific approach to address a particular exposure metric appropriately. The assessment approaches and tools to be used in each tier of analysis are summarized in Table 1. This three-tiered approach is designed to be both informative and cohesive such that each progressive tier builds upon efforts in the previous tier(s). For example, results of the air quality analysis (Tier I) will identify which particular urban areas or regions might be analyzed further in subsequent tiers. It should be noted that progression to higher tier levels, while reducing the overall span of the analysis, increases the level of spatial and temporal detail in the generated exposure results. Specific objectives, tool applications, assessment inputs and outcomes of each tier are described in greater detail below.

Table 1. Summary of Metrics and Tools Used for each Tier of the NO_2 Exposure Assessment.

	Exposure Metrics and Tools Used	
Tier	**Short-Term (hourly average)**	**Long-Term (annual average)**
AQ Characterization	AQ, Supplemental Data	AQ, Supplemental Data
Screening Exposure Assessment	AQ, MOBILE6, AERMOD, Population Weighting	AQ, HAPEM6
Refined Exposure Assessment	AQ, MOBILE6, AERMOD, APEX	AQ, MOBILE6, AERMOD, APEX

Notes
AERMOD American Meteorological Society (AMS)/EPA Regulatory Model
APEX EPA's Air Pollutants Exposure Model, version 4
AQ Air quality monitoring data
HAPEM6 EPA's Hazardous Air Pollutant Exposure Model, version 6
MOBILE6 EPA's mobile source emission factor model, version 6

At each tier of the exposure assessment, an evaluation of the uncertainties will be performed and the relative degree of confidence in the exposure estimates will be determined. Similar to the exposure assessment approach briefly described above, a tiered approach will be employed that begins with a qualitative uncertainty analysis and progresses to a quantitative analysis only if warranted and if data are available to support such an analysis. The first step in the uncertainty analysis would be to identify the components of the assessment that do or do not contribute to uncertainty, and provide a rationale for why this is the case. A qualitative evaluation would follow for the uncertain components of the assessment, resulting in a matrix describing, for each area of uncertainty, both the magnitude (minimal, moderate, major) and the direction of influence (under- or over-estimate) on exposure estimates. If sufficient data are available and if the magnitude of uncertainty is judged significant, a quantitative assessment of uncertainty would then be performed for selected components of the assessment.

3.2 POPULATIONS MODELED

A detailed consideration of the population residing in each modeled area would be included, where exposure modeling is performed. The assessment would not only include the general population residing in each modeled area but would also consider susceptible and vulnerable populations as identified in the ISA. These could include population subgroups defined from either an exposure or health perspective. The population subgroups identified by the ISA (US EPA, 2007b) that we plan to include in an exposure assessment include:

- Children (birth to age 18)
- Asthmatic children (birth to age 18)
- Asthmatic adults (>19 years)
- Elderly (≥65 years)

The proportion of the population of children characterized as being asthmatic will be estimated by statistics on asthma prevalence rates recently used in the NAAQS review for O_3 (US EPA, 2007e). Where sufficient data are available, region-specific data would be applied. In addition to these population subgroups, individuals anticipated to be exposed more frequently to NO_2 will be considered, including those commuting on roadways and persons who reside near major roadways.

3.3 TIER I: AIR QUALITY CHARACTERIZATION

The first step in assessing exposure will be to conduct an air quality analysis relying largely on ambient air quality data and the information provided in the ISA and relevant Annexes. In this type of analysis, the ambient NO_2 concentrations will serve as a surrogate for total human exposure and would allow a comparison with the results of the assessment performed for the 1995 NO_2 NAAQS review. This analysis would include information on NO_2 properties, current NO_2 air quality patterns, historic trends, local sources, and any potential concentrations of concern based on the ISA's evaluation of the health effects evidence. The relationship between short- and long-term averaging times will be evaluated and used to inform subsequent analyses of the current standard and any potential alternative standards that may be under consideration.

The four objectives in this analysis are to: (1) identify geographic locations (i.e., individual cities/combined metropolitan statistical areas [CMSA]) or groupings of similar areas of potential concern, (2) estimate short- and long-term surrogate exposure metrics, (3) develop a statistical model to estimate relevant surrogate exposure metrics assuming ambient levels of NO_2 just meet the current standard and potential alternative standards, and (4) estimate potential impact of important local sources on exposure surrogate metrics.

All available ambient monitoring data collected since the prior NO_2 NAAQS review (i.e., between 1995-2006) have been gathered for use in this assessment and will be used as is. Modification of air quality data is not required to analyze any alternative standards that may be under consideration, because parameters in the statistical model(s) developed would allow for a range of alternative standards to be evaluated. While ambient NO_2 concentrations have declined over this time period and there are no locations that are not meeting the current standard (Figure 1), the historical data are useful for characterizing ambient concentrations that were near or at the current standard level.

3.3.1 Approach

The first step in this analysis is to identify similarities and differences in air quality among locations for the purpose of either aggregating or segregating data based on the approach criteria. *Location* in this context would include a geographic area that encompasses more than a single air quality monitoring (e.g., city or CMSA). Based on initial analysis of air quality trends, availability of ambient NO_2 data (i.e., completeness of data, number of monitors), population demographics, location of NO_2 field and epidemiological health studies, and the desire to represent a range of geographic areas, the following CMSAs are planned to be assessed in this Tier as individual urban area locations:

- Los Angeles
- Houston
- Atlanta
- Philadelphia
- Chicago

Additional locations of interest (if any) will be identified through statistical analysis of the ambient NO_2 air quality data. The analysis will identify locations in excess of the 90th percentile of various metrics estimated using the ambient monitoring data and other information. The following analyses will be performed by year at each individual monitor:

- Annual average ambient concentrations
- Frequency of hourly peak concentrations above potential health effect benchmarks
- Hourly peak-to-annual mean ratios
- Number of hours of exceedances per day (for assessing multiple exceedances per day, including consecutive hour exceedances)
- Motor vehicle traffic density on major roadways (by location, not monitor)

The individual monitors identified from this first analysis will be aggregated by year at each CMSA/city regardless of whether a single or multiple monitors within a particular location were identified. The distributions of hourly ambient concentration and hourly peak-to-mean ratios for each location will be compared using visual (e.g., Q-Q plots[2]) or distribution testing

[2] Quantile-quantile (Q-Q) plots are useful for comparing ordered values of a variable with quantiles of a specified theoretical distribution.

(e.g., Kolmogorov-Smirnov (KS)[3]) to determine if additional aggregation of the air quality data is appropriate.

The analyses above will include both spatial (between and within cities) and temporal (within-city monitors by year) comparisons, where appropriate data are available. It should be noted that there may be statistically significant within-location differences due to the geographic placement of the monitors (e.g., near-roadway vs. not near a roadway). These within-location differences are important in explaining spatial variability in a particular location but are not to be used in this analysis to separate within-location monitors. However, spatial attributes of each monitor would be noted, such as whether the monitor is in close proximity to a major road or other important emission source of NO_2. In addition, monitors would be identified for use as potential background NO_2 concentrations within selected locations.

Air quality analyses already performed and reported in the ISA (US EPA, 2007b) includes correlations of monitors within individual cities (i.e., New York, Los Angeles, Houston, Baton Rouge, Chicago, Atlanta, for ambient monitoring conducted during the years 2003-2005). These analyses generally indicate strong positive within-location monitor correlations. All other ambient monitoring data not separated by the above analyses will be aggregated into one group, similar to what was done in the prior review (McCurdy, 1994).

The next step in this assessment is to develop new prediction equations for each location identified by the above analyses. The purpose of these new equations is to estimate frequency of short-term exposures, considering just meeting the current standard and any alternative standards under consideration. Previously, McCurdy (1994) performed an analysis of 1988-1992 air quality data to quantify the relationship between long-term average and short-term peak concentrations for the 1995 NO_2 NAAQS review. Linear and non-linear approaches were evaluated, with the non-linear regressions determined more appropriate. An exponential equation was used, of the general form:

$$y = \exp(a + bx) \qquad \text{eq (1)}$$

where,

y = dependent variable, number of exposures above a particular level (unitless)
a = estimated constant
b = estimated regression coefficient
x = independent variable, valid annual average ambient concentration (ppm)

McCurdy (1994) identified two locations, the Los Angeles CMSA and CMSA at all other sites across the U.S., and considered short-term concentrations of 0.15, 0.20, 0.25, and 0.30 ppm, 1-hr average, and annual average concentrations of 0.02, 0.03, 0.04, 0.05, 0.053, and 0.06 ppm. Estimated mean number of exceedances of the short-term concentrations, when just meeting the current standard and alternative annual average concentrations, are summarized in Table 2.

[3] The Kolmogorov–Smirnov (KS) test is a nonparametric test used to judge whether two ordinal-scale samples have the same continuous distribution, as would be expected if they were drawn from the same population (SAS, 2007). While it requires that the samples be independent and random, it does not assume any particular sampling distribution form. The test statistic is the maximum distance between cumulative distributions of the two samples (D_N) and the null hypothesis (H_0) of no difference in the distributions is rejected when D_N becomes too large as evaluated by a χ^2-test at α=0.05.

Results of the McCurdy (1994) analysis indicated that most locations in the U.S. would have limited or no exceedances of any short-term exposure level considered, with limited exceedances occurring in Los Angeles given just meeting the current standard as an example.

Table 2. Estimated Number of Short-Term Concentrations Above Various Levels Given Annual Average Concentrations Using 1988-1992 Ambient Monitoring Concentrations (McCurdy, 1994).

Annual Average (ppm)	**0.15 ppm-1hr**		**0.20 ppm-1hr**		**0.25 ppm-1hr**		**0.30 ppm-1hr**	
	LA[a]	**Others[b]**	**LA**	**Others**	**LA**	**Others**	**LA**	**Others**
0.02	4	2	0	0	0	0	0	0
0.03	9	3	0	0	0	0	0	0
0.04	33	4	1	0	0	0	0	0
0.05	57	5	7	0	1	0	0	0
0.053	75	5	13	0	1	0	0	0
0.06	142	7	38	0	5	0	0	0

Notes
[a] LA is the Los Angeles CMSA
[b] Others is all other CMSA across the U.S.

Exponential regression equations will be developed in this Tier similarly, using the air quality data obtained from 1995-2006. Preliminary analysis of the recent air quality data for the U.S. (years 2001-2005) indicate that a non-linear relationship exists between the number of short-term concentration exceedances and the annual average concentration, and this is consistent with the findings of McCurdy (1994). It may be that location-specific equations are required, a result of potential variation in the relationship between the short-term peak concentration to long-term averages, and possibly across different years. This would be investigated by comparing regression models, parameters, and respective concentration exceedance estimates derived from early monitoring data (e.g., 1995-2000) versus those using more recent air quality monitoring data (e.g., 2001-2006).

The regression model is highly dependent on the prevalence of concentration exceedances, justifying the aggregation of particular (and similar) locations. In contrast, frequency of occurrence also may be distinct, as McCurdy (1994) observed with the above results for LA, justifying the separation of locations to develop area-specific prediction equations. While it may seem ideal for all data to be included in the analysis, standard criteria exist for inclusion of a given monitor in that it contains a valid annual data set.[4] Model and parameter significance will be assigned at $P<0.05$, with the model explanatory power evaluated by a Fisher's-exact test and adjusted R^2. In addition, all results, including predictive equations and exceedance estimates will be compared with that reported by McCurdy (1994), where appropriate comparisons can be made.

3.3.1.1 Mobile Source Influence

As an additional step in this air quality analysis, the potential impact of local sources on the surrogate exposure metrics will be evaluated. Motor vehicles can be a significant outdoor

[4] A valid year is comprised of 75% of valid days in a year, with at least 18 hourly measurements for a valid day (thus at least 274 valid days, a minimum of 4,932 hours)

emission source of NO_x. Using data provided in the Chapter 2 ISA Annex, Table AX2-3, highway vehicles are noted as the largest single source category contributing to the total estimated NO_x emissions for the U.S. (Figure 2).

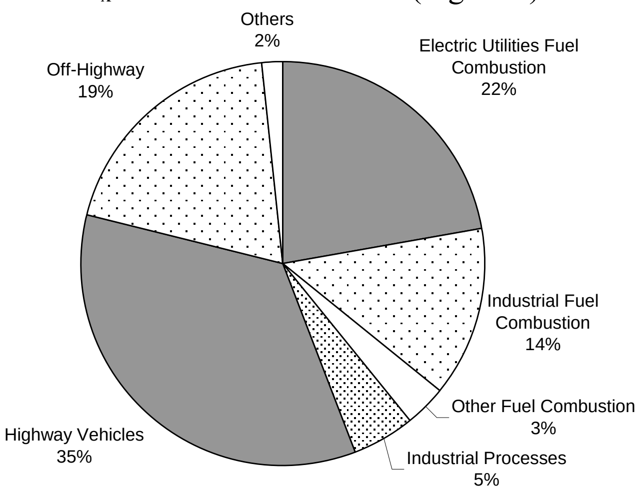

Figure 2. Percent of Total NO_x Emissions in the United States by Major Source Categories.

Several studies have shown that concentrations of NO_2 are at elevated levels when compared to ambient concentrations measured at a distance from the roadway (e.g., Rodes and Holland, 1981; Gilbert et al., 2003; Cape et al., 2004; Pleijel et al., 2004; Singer et al., 2004). On average, concentrations at or near a roadway are from 1.5 to 2 times greater than ambient concentrations (US EPA, 2007b), but on occasion, as high as 7 times greater (Bell and Ashenden, 1997; Bignal et al., 2007). A strong relationship between NO_2 concentrations measured on roadways and those with increasing distance from the road has been reported under a variety of conditions (e.g., variable traffic counts, different seasons, urban versus rural locations) and is best described with an exponential decay equation of the form

$$C_x = C_b + C_v e^{-kx} \qquad \text{eq (2)}$$

where,

C_x = NO_2 concentration at a given distance (x) from a roadway (ppm)
C_b = Background NO_2 concentration (ppm)
C_v = NO_2 concentration contribution from vehicles on a roadway (ppm)
k = Rate constant describing NO_2 combined formation/decay with perpendicular distance from roadway ($meters^{-1}$)
x = distance from roadway (meters)

As a function of reported concentration measures and the derived relationship, much of the decline in NO_2 concentrations with distance from the road has been shown to occur within the first few meters (approximately 90% within 10m distance), returning to near ambient levels between 200 to 500 meters (Rodes and Holland, 1981; Bell and Ashenden, 1997; Gilbert et al., 2003; Pleijel et al., 2004). At a distance of 0 meters, referred to as *on-road* here, the equation simply reduces to the sum of the background NO_2 concentration and the concentration contribution expected by vehicle emissions on the roadway. Based on data available in these studies and other published studies on the concentration decay with distance from roadways, a relationship would be developed and used to modify the existing ambient monitoring data to estimate roadway NO_2 concentrations in study areas, using

$$C_r = C_a + mC_a \quad \text{eq (3)}$$

where,

C_r = On-road NO_2 concentration (ppm)
C_a = Ambient monitor NO_2 concentration (ppm)
m = Ambient modification factor (unitless)

The parameter *m*, will be derived from the relationship between the C_v and C_b estimates (from eq (2) above), either in the form of a ratio (C_v/C_b) or by using linear regression (regress C_b on C_v, and then using the derived slope for the multiplier on C_a which would then be added to the estimated model intercept). Depending on the amount and type of data available, the ratio may be in the form of a distribution to be sampled from or the linear regression parameter errors may be incorporated to represent variability in on-road concentrations. The on-road parameter(s) will also include known influential factors (e.g., traffic counts, seasonal differences), where relevant data are available.

Both long- and short-term metrics will be estimated using the on-road NO_2 concentrations, as described above for the ambient monitoring data. This includes the estimation of annual average concentrations and use of equation (1) to estimate the number of short-term concentrations above selected levels that could occur on roadways using the hourly C_r values, associated with just meeting the current standard and any potential alternative standards that may be considered. It should be noted that near-roadway concentrations are not estimated in this Tier I assessment since they would be expected to fall somewhere between the ambient and on-road concentrations.

3.3.1.2 Stationary Source Influence

Power generating utilities and related processes are estimated as the next greatest major source of NO_x emissions, contributing to 22% of total NO_x emissions (see Figure 2). Analysis of the 2002 National Emissions Inventory (NEI) indicates fossil fuel electrical utilities (NAICS[5] code 221112) alone comprise 42% of the total nationwide NO_x emissions for stationary sources, with transmission and distribution activities (NAICS code 2211) contributing the next greatest percentage of 8.5%. Due to national and local site distribution, these are important sources to estimate any additional concentration contributions that may occur locally within selected study areas. Other stationary NO_x emission sources may be identified as being important, based on consideration of local emissions estimates. For example, analysis of Los Angeles county emissions from the NEI indicates that the principal sources of NO_x locally are petroleum refineries (28.8%), support activities for air transportation (26.9%), followed by contributions from fossil fuel utilities (11.8%). Available data for ambient concentrations estimated near these sources in the selected study areas would be used to estimate the potential influence on long-term and short-term air concentrations as described above, considering times of source operation and other influential factors, where appropriate.

[5] North American Industry Classification System (NAICS).

3.3.1.3 Indoor Source Influence

The ISA (Chapter 2) indicates that indoor sources of NO_x are a significant contributor to personal exposures. Important indoor sources include those operating through the combustion of fossil fuels, particularly natural gas cooking appliances (e.g., stoves and/or cooktops), gas fireplaces, and space heaters. Biomass combustion (e.g., wood stoves and fireplaces) and environmental tobacco smoke were noted as having insignificant to limited contribution to indoor concentrations, particularly if properly vented.

Available data for indoor concentration distributions or emissions from the important sources would be used to estimate the potential influence on long-term and short-term air concentrations as described above, considering times of source operation, frequency of use, and any other influential factors (e.g., vented versus not vented), where appropriate.

3.3.2 Generated Outcomes

Descriptive statistics (e.g., annual average concentrations, peak-to-mean ratios) and statistical outcomes (e.g., distributions and inter/intra site comparisons, common/distinct locations identified based on ambient air quality distributions) will be summarized in tables and figures, accounting for particular factors contributing to their variability (e.g., year, location). In addition, exposure metrics will be generated using relationships derived from ambient monitor and other data. Estimated regression equations will, at a minimum, allow for the estimation of a mean number of exceedances of several short-term peak concentrations (e.g., 1-hour exceedances ranging from 0.15 to 0.25 ppm) upon just meeting the current annual NO_2 standard and meeting other potential alternative standards that may be under consideration. In addition, prediction intervals around the mean estimates will be approximated to provide lower and upper limits, bounded by a minimum of 0 and maximum observed values where prediction intervals exceed these values. For example, Table 3 contains such estimates of the number of exceedances 0.15 ppm, 1-hr average in Los Angeles, based on a preliminary non-linear regression analysis of year 2001-2006 ambient data for Los Angeles County.

In addition to determining whether local patterns in air quality are similar/unique compared to other locations and developing new predictive equations, the analysis will assist in identifying Tier II and III areas to be modeled, if needed. Spatial attributes of monitors will also be identified for assigning ambient concentrations in the Tier II and III exposure assessments appropriately.

Table 3. Estimated Number of NO_2 Concentrations in Los Angeles, CA Above 0.15 ppm, 1-hr Average Given the Annual Average Concentration Using 2001-2006 Ambient Monitoring Concentrations.

Annual Average (ppm)	Number of Exceedances of 0.15 ppm-1hr[a]		
	Lower Bound	Mean	Upper Bound
0.020	0	0	6
0.025	0	0	57
0.030	0	0	559
0.035	0	0	[c]
0.040	0	2	[c]
0.045	0	11	[c]
0.050	0	57	[c]
0.053	0	154	[c]

Notes
[a] Los Angeles county only (code 037).
[c] Extrapolation outside of the range of the mean air quality data can result in extremely large estimates for the upper bound 95th percentile prediction interval. Note that the actual maximum number of measured exceedances was 6 given an annual average concentration of about 0.040 ppm.

3.3.3 Variability and Uncertainty

One general assumption regarding the air quality characterization is that the air quality data used are quality assured already. Reported concentrations contain only valid measures, since values with quality limitations are either removed or flagged. Therefore, the air quality data used contributes minimally to uncertainty. Temporally, the data are hourly measurements and appropriately account for variability in concentrations that are commonly observed for NO_2 and by definition are representative of an entire year. In addition, having more than one monitor does account for some of the spatial variability in a particular location. However, the degree of representativeness of the monitoring data used in this analysis can be evaluated from several perspectives, one of which is how well temporal and spatial variability are represented. Other concerns could be the exclusion of any unidentified outdoor sources, the ability of ambient monitors to capture the effect of local sources, and the effect of local sources on personal exposure estimates. Additionally, there is uncertainty in the application of the identified potential health effect benchmark levels to exposure estimates for both the general population and for those potentially susceptible individuals.

As mentioned in the overview, a tiered approach to assessing uncertainty will be employed with the goal of progressing to a quantitative analysis if warranted and if data are available to support such an analysis. The first step in the uncertainty analysis would be to identify the components of the assessment that do or do not contribute to uncertainty and to provide a rationale for why this is the case. This is described below for this particular Tier of the assessment, although the identified components are, in a broad sense, also relevant to subsequent exposure analyses. The following includes a preliminary qualitative evaluation for the uncertain components of the planned Tier I analysis, indicating the direction of influence (under- or over-estimate) on exposure estimates.

- Ambient NO_2 measurement: Uncertainty in the ambient measurement of NO_2 due to interference with other oxidized nitrogen compounds. The ISA points out positive interference, commonly from HNO_3, of up to 50%, particularly during the afternoon hours, resulting in overestimation of concentrations. Also negative vertical gradients exist for monitors (2.5 times higher at 4 meter vs. 15 meter vertical siting (see the ISA)), thus monitors positioned on rooftops may underestimate exposures. It should also be noted that use of the older data in some of the analyses here carries the assumption that the sources present at that time are the same as current sources, adding uncertainty to results if this were not the case.
- Temporal Representativeness: Data are valid hourly measures and should be of the same temporal scale as identified potential health effect benchmarks. While there may be missing values within a given valid year contributing to uncertainty (data will not be interpolated in this Tier analysis), temporal profiles will be assumed complete and representative for this Tier I analysis.
- Spatial Representativeness: In general, there only a few to several monitors in a given area. Since most locations have sparse siting, the monitoring data will be used for both spatial interpolation (for the area between monitors) and extrapolation (for locations distant from monitors and to represent local sources). Among area monitors, high correlations could indicate spatial representativeness for ambient concentrations, while low correlations might indicate the presence of local sources and thus heterogeneity in ambient concentrations. The impact of monitor spatial representativeness on the prediction equations could be assessed by evaluating the impact of each given monitor to parameter values and resultant exceedance estimates. Spatial variability in collective remote/distant monitors could be evaluated through correlation testing and may indicate that limited uncertainty exists in the extrapolation to areas at great distances to ambient monitors. When local sources are present and not represented well by distant ambient monitors, there may be significant uncertainty with limited quantitative measures.
- Monitor to Exposure Representativeness: Human exposure is characterized by contact of a pollutant with a person, and as such, this analysis contains the broad assumption that the monitors are representing that contact in some form. While some longer-term personal exposure data may be available for development and evaluation of a relationship, short-term personal exposures are typically not measured. Therefore the relationship of peak-personal (i.e., attributed to ambient) to peak-ambient is largely unknown and thus contributes to uncertainty. There might not be a method to assess quantitatively the impact of the uncertain relationship between ambient monitors and personal exposures on the Tier I estimates, particularly since measured personal exposures are typically time-averaged over days rather than hours. An evaluation provided in the ISA and Annexes indicates that the relationship between ambient concentrations and personal exposures ranges from poor to good (r_p: 0.06 to 0.86), and is generally improved in the absence of indoor sources.
- Roadway to Ambient Monitor Relationship: Roadway and ambient monitoring concentrations have been shown to be correlated significantly on a temporal basis (e.g., Cape et al., 2004) and motor vehicles are a significant emission source of NO_x, providing support for estimating on-road concentrations using ambient monitoring data. The relationship used would be derived from studies with mostly long-term averaging times, typically 14-days or greater in duration (e.g., Roorda-Knape, 1998; Pleijel et al., 2004;

Cape et al, 2004), although one study was conducted over a one-hour time averaging period (Rodes and Holland, 1981). This is considered appropriate for estimating hourly values from hourly ambient measures, assuming a direct relationship exists between the short-term peaks to time-averaged concentrations (e.g., hourly roadway NO_2 concentrations are correlated with 24-hour averages). While this should not impact the overall contribution relationship between vehicles and ambient concentrations on roads, the decay constant k will differ for shorter averaging times. This could result in either over- or under-estimates of near-road concentrations, if short-term concentrations are estimated at a distance from the road (not planned here). The on-road concentration estimation assumes that concentration changes that occur on-road and at the monitor are simultaneous (i.e., within the hour time period of estimation). The long-term data used to develop the model were likely collected over variable meteorological conditions (e.g., shifting wind direction) and other influential attributes (e.g., rate of transformation of NO to NO_2 during the daytime versus nighttime hours) than would be observed across shorter time periods. Furthermore, on-road concentrations are not modified in this Tier to account for in-vehicle penetration, possibly resulting in an overestimate in on-road concentrations, given that while non-reactive pollutants such as benzene or carbon monoxide have been shown to have comparative concentrations inside vehicles compared with outside, reactive pollutants (e.g., $PM_{2.5}$) tend to have a lower indoor/outdoor concentration ratio (Rodes et al., 1998). At locations where traffic counts are very low (e.g., on the order of hundreds/day) the roadway contribution has been shown to be negligible (Bell and Ashenden, 1997; Cape et al., 2004), therefore any rural areas meeting the standard with minimal traffic volumes would likely result in small overestimations of NO_2 concentrations using eq (3). For monitors that have been characterized as within close proximity of the roadway (<10m), on-road concentrations would likely be overestimated using eq (3).

- Potential Health Effect Benchmark Representativeness: Health effect benchmarks will be based on the assessment of the science as documented in the ISA. The choice of specific health effect benchmarks could introduce additional uncertainty into the exposure analysis. For example, uncertainties in the exposure characterization and/or in the susceptibility of specific populations could contribute to the overall uncertainty. We anticipate that any uncertainties added by the health effect benchmarks will be discussed qualitatively based on information provided in the ISA.

3.4 TIER II: SCREENING-LEVEL EXPOSURE ASSESSMENT

A screening-level exposure assessment would be designed to represent the relationship between ambient concentrations, local sources, and human exposure. The approach would involve the development of screening-level exposure metrics to estimate variability in human exposure by considering time spent in various locations, rather than assuming that ambient concentrations are equivalent to exposures. Two objectives of the approach, building upon the analysis performed in the Tier I assessment, are to improve the spatial resolution of the ambient concentration fields, and to simulate human contact with NO_2.

The screening-level exposure assessment would be conducted in the CMSA's locations identified in the Tier I air quality characterization, and would use recent year ambient monitoring concentrations (e.g., 2004 to 2006). The approach may also include assessing exposures in an area with relatively low NO_2 levels that is not influenced by significant local sources or transport to provide an example of a possible lower bound estimate, if a location can be identified that meets these criteria. This screening-level exposure assessment would incorporate important influential factors, including those listed below:

- Factors that contribute to greater personal exposures (short- and long-term), including the impact of important sources of NO_2 (e.g., vehicle emissions) and the impact of human behavior (e.g., time spent outdoors, time spent on- or near-roadways)
- Factors that contribute to lessened personal exposures (short- and long-term) to ambient NO_2, including the decay of NO_2 indoors and the time spent indoors and inside vehicles.
- Population living within the screening-level exposure region
- Number of exposures of concern experienced by potentially susceptible populations (e.g., asthmatics) relative to those experienced by the general public within the region.

Two separate approaches will be taken to assess short-term peak and long-term average exposures, although some of the technical details for each will overlap, and thus the approaches will remain comparable. Both approaches will begin with the spatial interpolation of ambient monitoring concentrations, i.e., assigning a census tract[6] concentration based on the nearest ambient NO_2 monitoring concentration. In addition, any missing hourly values within the ambient monitoring data will be approximated, using either linear interpolation between the valid values at the ends of the missing data gap or linear regression models developed from nearby ambient monitors. The result will be a complete set of hourly ambient NO_2 concentrations for all tracts within the modeled area. Then, for short-term peak exposures, improvement in the spatial resolution of NO_2 concentrations will be accomplished through a combined emissions and dispersion modeling approach. For long-term exposures, an exposure model that accounts for proximity to local sources will be used to adjust ambient NO_2 monitoring concentrations. Both of these are discussed in detail below.

3.4.1 Short-term Exposure Approach

The first step is to enhance the existing hourly air quality data given that there may be locations people visit that are not well represented by an ambient monitor. When considering important local sources of NO_2, it is anticipated that short-term peak concentrations will be higher on or near roadways, therefore a focus of this approach is centered upon improving the estimation of NO_2 concentrations within a given distance to roadways. These on- and near-roadway concentrations would be combined with the NO_2 ambient monitoring concentrations to represent the spatial variability of NO_2 in the study location.

The approach for estimating short-term peak concentrations on- and near-roadways would use two models, MOBILE6, an emissions estimating model, and AERMOD, an atmospheric dispersion model. MOBILE6 is the U.S. EPA's mobile source emission factor model used to estimate emission rates for motor vehicles while accounting for variables such as ambient temperatures, travel speeds, operating modes, fuel volatility, and mileage accrual rates (US EPA, 2003). A GIS-based approach will be used here to develop spatially resolved linked-

[6] Census tract level demographic data obtained from the US Census database has been commonly used in exposure assessments for characterizing particular attributes of a population (e.g., age, gender, work status) in a selected study area.

based emissions for major roads[7], using road link locations from the TIGER ROAD network combined with traffic activity for each road link in the form of traffic volumes from State/Local metropolitan planning agencies or from regional travel demand models (e.g., TRANPLAN, DTIM). Hourly emission rates of NO_2 would be estimated based on modification factors developed from daily, weekend/weekday, and monthly driving patterns[8]. Then, the local near-road pollution gradients can be approximated using these link-based emission estimates as input to AERMOD, a steady-state, Gaussian plume model (US EPA, 2004).

Census tracts containing major roads will be assigned NO_2 concentrations for portions of the tract that are within a particular distance from the roadway (i.e., the portion of the block group located within 75 meters (m) of the roadway, and/or within 75-200m)[9]. These concentrations will be estimated by averaging AERMOD receptor concentrations generated within the specified buffer region. Nitrogen dioxide concentrations for portions of census tracts >200m or where the entire tract is >200m from a roadway will be assigned the nearest ambient monitoring concentration, subject to the constraint that the nearest monitor is not within 200m of a major road (i.e., assumed to not be greatly influenced by roadway emissions). The final product will be a data set containing hourly NO_2 concentrations for each census tract in the study location(s) for each of three roadway proximity classes (i.e., <75m, 75-200m, >200m) and hourly on-road concentrations for the tract containing major roadways, where appropriate.

If additional sources are identified in the Tier I assessment as potentially important contributors to ambient air concentrations in a selected area (e.g., emissions from electric power utilities, petroleum refineries, airports, gas pumping stations), then emissions from these sources would be used in AERMOD to estimate the additional concentration contribution in each individual roadway proximity category, where such sources exist given their location within a census tract.

The second step is to simulate contact of ambient NO_2 with people, focusing on estimating the frequency of potential exposures of concern (EOC) (Figure 3). The frequency of short-term EOC would

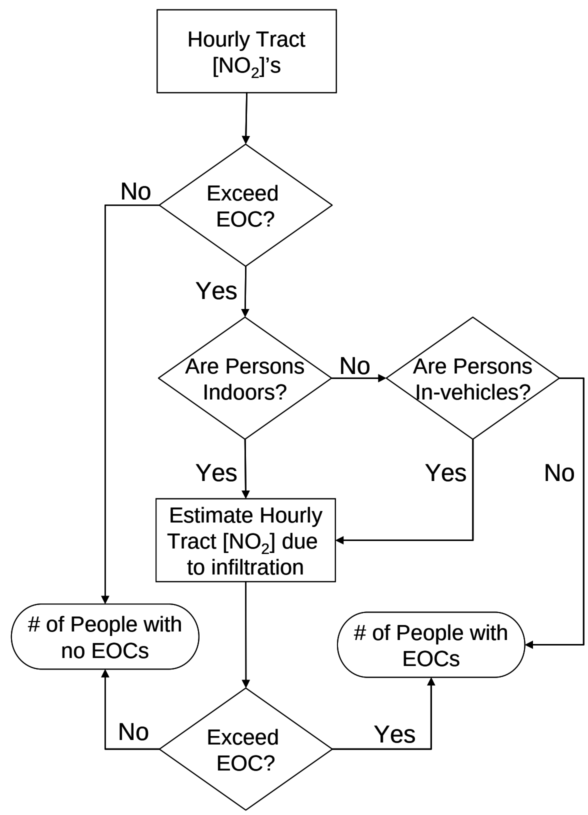

Figure 3. Decision Flow for Tier II Screening-level Approach in Estimating the Number of Person-occurrences of Short-term Exposures of Concern (EOC).

[7] Major roads will be identified in each simulated location by the Census Feature Class Codes (CFCC). These include "Limited Access Highway", "Highway", "Major Road", or "Ramp".
[8] Since >90% of mobile source NO_x is emitted as NO and the reaction rate is rapid, conversion rates could be determined using seasonal average ozone data and a simple reaction rate constant. Alternatively, CALINE4, with its limited NO_2 chemistry could also provide a reasonable approximation.
[9] The data for the fraction of the tract area within given distances of roadways as well as the fraction of the tract population within given distances is available within HAPEM6 data files (US EPA, 2007c). Current default age categories for the population residing near major roads are 0-1, 2-4, 5-15, 16-17, 18-64, and 65+ years in age.

be estimated using the fraction of people residing in the tract that are within distances of major roadways and the probability of time spent outdoors/indoors/in-vehicle for specific times-of-day and days-of-week. The analysis proceeds as follows, for any selected EOC.

The newly estimated tract on- and near-road concentration fields for each location are first screened for where and when concentrations are in excess of potential EOC. If there are no exceedances in a tract at any of the three designated distances from roadways or on the roadway, then the tract is estimated to have no persons with potential EOC. Where there are exceedances, data for time spent in three locations (indoors, inside vehicles, and outdoors) would be used to estimate the fraction of the population residing in that census tract that might be in direct contact with the EOC. This would be determined from population-based hour-of-day time spent in a particular location (e.g., fraction of population with time indoors at specific hours) extracted from time-location-activity diary data in EPA's Consolidated Human Activity Database (CHAD) (McCurdy, 2000). For the fraction of the tract population residing indoors at a particular hour and for each roadway proximity class, the outdoor concentrations will be adjusted using an infiltration factor[10] to estimate the corresponding indoor NO_2 concentrations of ambient origin. The proportion of the population not indoors would then be assigned either on-road concentrations (adjusted with an infiltration factor, where relevant data exist), or outdoor concentrations (for each respective proximity class). The population may be disaggregated based on specific age cohorts given the inherent variability in the time spent outdoors (Graham and McCurdy, 2004) and/or any subgroups identified below as potentially susceptible to NO_2 exposure. The total number of persons with EOC, whether through indoor, in-vehicle, or outdoor contact, can then be estimated for the population in the tract over the specified time period of analysis.

If indoor sources are identified in the Tier I analysis as potentially important contributors to ambient air concentrations in a selected area (e.g., gas appliances), then emissions from these sources would be used to estimate an additional concentration contribution to the indoor environment. The process would begin as described above, however there would not be an initial screen of the set for census tracts with no exceedances (see Figure 3). This is because the added contribution of indoor sources could potentially raise the exposure concentration above a level of concern, where previously the tract would have been screened out of the assessment. An additional step would be added to the estimated indoor exposure concentration that accounts for the population frequency of use, time of use, and indoor concentrations associated with emissions from particular gas appliances.

To summarize, the Tier II exposure analysis would synthesize three data sets to estimate short-term exposure metrics (see Figure 4), (1) a *concentration set* containing census tract hourly concentrations at each of three distances from major roads developed from ambient monitoring concentrations and modeled on-road concentrations (and additional outdoor sources, if any), (2) a *tract set* containing the fraction of the tract population and tract areas within 3 roadway distance categories (already available from HAPEM6), and (3) a *parameter set* containing

[10] Would be obtained from the Chapter 3 Annex, in the form of an infiltration factor (F = [Pen*ach]/[ach+k]) or ratios of indoor/outdoor NO_2. The same equation would apply to in-vehicle infiltration, provided specific data are available.

indoor, outdoor, in-vehicle time probabilities, infiltration factors for indoor and in-vehicle environments, and various indoor source parameters.

Concentration Set

TractID	Year	Month	Day	Hour	Conc>200m	Conc75-200m	Conc<75m	ConcOnroad
0401300191	2004	3	9	09:00	0.090	0.090	0.091	0.155
0401300191	2004	9	24	08:00	0.088	0.088	0.089	0.151
0401330101	2004	1	6	08:00	0.103	0.103	0.104	0.177
0401330101	2004	1	6	09:00	0.104	0.104	0.105	0.179
0401330101	2004	11	5	06:00	0.088	0.088	0.089	0.151
0401330101	2004	11	5	07:00	0.103	0.103	0.104	0.177
0603711031	2004	8	7	09:00	0.090	0.094	0.132	0.181
0603711031	2004	8	31	08:00	0.081	0.084	0.118	0.162
0603711031	2004	8	31	09:00	0.101	0.106	0.150	0.203
0603711031	2004	8	31	10:00	0.087	0.091	0.127	0.174
0603711031	2004	9	1	08:00	0.088	0.088	0.089	0.151
4814100441	2004	6	2	08:00	0.083	0.086	0.121	0.166

Tract Set

TractID	Pop	Pop>200m	Pop75-200m	Pop<75m	TotalArea	Area>200m	Area75-200m	Area<75m
01001020100	368	1.000	0	0	457	1	0	0
01001020200	1027	0.0058	0.1334	0.8608	328	0.1693	0.2142	0.6165

Parameter Set

Variable	Value
TimeIn1	0.97
TimeIn2	0.97
TimeIn3	0.98
TimeIn4	0.97
TimeIn5	0.94
TimeIn24	0.96
TimeOut1	0.03
TimeOut2	0.02
TimeOut3	0.02
TimeOut4	0.02
TimeOut5	0.03
TimeOut24	0.03
F_{in}	0.55
F_{veh}	0.91

Figure 4. Illustration of Basic Data Required to Estimate Number of Person Occurrences of Short-term Exposures in a Tier II Exposure Assessment. Complexity of Data Structure is Dependent on the Number of Population Subgroups and Day-Types Modeled.

3.4.1.1 Generated Outcomes

Outcomes of this analysis would include, temporally and spatially resolved ambient concentrations for selected locations that account for local mobile and stationary source emissions, and the number of simulated person occurrences of EOC per year (or other time frame of interest) disaggregated to particular population demographic subgroups in each location. These outcomes would be generated for current NO_2 levels as well as levels just meeting the current and any potential alternative standards under consideration. An example of exposure model output for each hour for a tract in a location is provided in Table 4, calculated using hypothetical values provided in Figure 4. Total exposure concentrations for the distance categories and tract are weighted by the number of individuals that spend time indoors, outdoors, and inside vehicles, considering particular distances from a roadway. The estimated exposures could also be aggregated for any number of time periods for a census tract/demographic group modeled (e.g., daily, 7-day, annual average for ages 0-2).

Table 4. Example of Anticipated Hourly Exposure Output for One Census Tract Using Tier II Assessment.

Exposure Metric[a]	Location	Road Proximity Class (meters)			Total Tract[b]
		>200m	75-200m	<75m	
Number of Person Occurrences > 0.150 ppm	Indoor	0	0	0	0
	Outdoor	0	0	18	18
	In-Vehicle	0	1	9	10
	Total	0	1	27	28
Average Concentration (ppm)	Indoor	0.055	0.058	0.083	0.079
	Outdoor	0.101	0.106	0.150	0.144
	In-Vehicle	0.185	0.185	0.185	0.185
	Total	0.041	0.061	0.086	0.081

Notes

[a] This example calculation used data from Figure 4, tract 0603711031, date 08-31-2003, hour 09:00.

[b] Total number of person occurrences are sums for the tract population. The total concentration data are population weighted exposure concentrations for the tract based on the fraction of the population in each location and/or proximity class.

3.4.1.2 Variability and Uncertainty

Improvements to capturing population variability and the reduction of uncertainty in NO_2 exposure estimates using the Tier II short-term exposure assessment include: (1) better representing the spatial variability in NO_2 ambient concentrations due to local mobile and stationary source emissions, (2) accounting for the number of persons and where they might reside with respect to location of potential exposure concentrations, (3) representing variability in time spent outdoors by considering influential factors such as time-of-day and day-type, and (4) simulating infiltration of outdoor concentrations to indoors and in-vehicle environments.

Limitations to the approach that contribute to uncertainty in the exposure estimates include: (1) individuals are not simulated, thus variability in exposure estimates is likely constrained, (2) population statistics for time spent indoors/outdoors/in-vehicles may not be applicable to the population simulated, which could result in under- or over-estimates in exposure, and (3) while elements of the time pattern of exposure are retained, individual behavior is not correlated with locations visited and hence specific concentrations experienced, which could result in under- or over-estimates in exposure metrics. For example, the model assumes the portion of the population when outdoors, is outdoors for the entire hour. This could lead to overestimation of exposure. There is no correlation from hour-to-hour for individuals, thus repeated peak exposures for individuals would be underestimated.

There may be uncertainty in the selected approach that estimates on- and near-road concentrations, the approach used for estimating concentrations in broad microenvironments, or the approach to approximate human contact with NO_2. As a first-level evaluation, model estimates will be compared to measurement data, where relevant data are identified and available. For example, the on- and near-road concentration estimates could be compared with measured ambient monitoring data where the siting location is within the roadway proximity categories. Modeled indoor and exposure concentrations could be compared with respective measurement data, although these data have only been collected in few locations in U.S. (US EPA, 2007b).

Other uncertainties in this Tier II Assessment could be assessed quantitatively through individual parameter analyses. For example, the method for interpolation of missing ambient monitoring data could be assessed in a manner similar to that used for the recent O_3 NAAQS (US EPA, 2007e; Langstaff, 2007). Also, the model could be run through several iterations for each tract with random sampling of time probabilities (using uncertainty intervals of +/-10%) and infiltration factors (accounting for variability in residence or building type) to develop bounds around exposure frequency estimates. Uncertainty in model structure would mainly be evaluated qualitatively; however, a quantitative assessment may be conducted by time-aggregating the short-term exposure estimates and comparing them with long-term exposure estimates generated below (Section 3.4.2).

3.4.2 Long-term Exposure Approach

The estimation of long-term exposures considering proximity to roadways will use ambient NO_2 data from 2004 through 2006 interpolated to census tracts in each of the study locations. The Hazardous Air Pollutant Exposure Model, version 6 (HAPEM6) will be used here as a screening-level exposure model to estimate long-term population exposures. Details on model inputs, algorithms, and outputs are provided in US EPA (2007c).

Briefly, HAPEM6 employs five principal data sets, the US Census population data, GIS information on roadway segments, human activity data from CHAD, air quality data, and microenvironment (ME) data, to estimate indoor, outdoor and in-vehicle exposures using a microenvironmental approach. The ME describes the physical location of an individual, allowing for direct contact with the immediate surrounding air that contains a homogeneous pollutant concentration. An example of a ME could be indoors at home, outdoors at a park, or in a vehicle. Individuals typically encounter many different MEs in the course of their activities over time. As a result, individuals will experience different pollutant concentrations in each of the MEs. Microenvironmental exposure models such as HAPEM6 simulate the variability in exposure by estimating the various concentrations that individuals encounter within a ME. In addition, several stochastic elements are incorporated into HAPEM6 to characterize variability in exposure, including simulating worker commutes, the representing of long-term activity patterns, and sampling from distributions of ME factors used to estimate the ME concentrations.

The current version of the model is designed to address three pollutant types, gases, particulates, and semi-volatiles. Microenvironmental factors have been estimated for each of these pollutant types for use in calculating ME concentrations, in general, as follows:

$$ME = PROX \times PEN \times Conc_{amb} + ADD \qquad \text{eq (4)}$$

where,

ME	=	estimated microenvironmental concentration (ppm or ppb)
$PROX$	=	proximity factor for microenvironment, literature derived ratio of outdoor ME concentrations to ambient concentration (unitless)

PEN	=	penetration factor for microenvironment, literature derived relation either as a ratio of indoor ME concentration to outdoor ME concentration, or from a linear regression (unitless)
$Conc_{amb}$	=	annual average ambient concentration for tract, could be stratified for time of day (ppm or ppb)
ADD	=	an additive factor that accounts for emission sources (indoor) within or near a ME (ppm or ppb)

The assignment of each census tract's ambient NO_2 concentration will be based on the nearest ambient monitoring concentration provided that the monitor is not within 200m of a roadway. Microenvironmental concentrations are estimated using eq (4), time-weighted based on daily activity patterns and day-types for a year (e.g., summer weekday, non-summer weekday, weekend), and combined to yield an annual average NO_2 exposure concentration for a cohort of interest (commonly defined by demographic attributes such as age and/or gender).

Since NO_2 is a gas, the HAPEM6 default ME factors for gases will be modified where NO_2 specific data are available. In the current version of HAPEM, there are 14 MEs for which concentrations can be estimated; however, data to develop factors for each of these MEs may be limited. It may be necessary to compress MEs into broad ME categories such as indoors, outdoors, and inside vehicles as done for the short-term approach. HAPEM6 can use ambient annual average concentrations stratified by time-of-day, therefore each census tract's hourly NO_2 concentrations will be averaged to give 24 1-hour average concentrations (i.e., a diurnal pattern). Rather than estimate on- and near-roadway concentrations as part of the air quality concentration field, HAPEM6 uses proximity factors to estimate concentrations for the MEs that are within the same three roadway distance categories described above. The estimation of these NO_2 specific proximity factor distributions will be important in the estimation of on- and near-road concentrations. The fraction of the population residing in the tract also described previously for the short-term exposures will be used here to estimate exposure within the same roadway distance categories. The impact from additional outdoor sources (e.g., power utilities) could also be considered in tracts where such sources exist, by using the concentrations estimated by AERMOD in the short-term Tier II assessment and using the appropriate averaging time.

Although some of the parameters in the default HAPEM6 files are designed for a specific age group (e.g., the fraction of the demographic within a certain distance of a major roadway), additional modification to parameters may be needed to allow for estimation of exposures for different age groups (e.g., susceptible subgroups identified in the ISA). Day-type definitions may also be tailored to specific geographic regions to match anticipated activity patterns in that study location, where relevant data are available (e.g., summer season duration in Houston versus that in Chicago). HAPEM6 also has an indoor source module that could be used to estimate the additional concentration contribution of these sources to estimated exposures through the *ADD* factor.

3.4.2.1 Generated Outcomes

HAPEM6 estimates annual average exposure concentrations for a tract that are weighted by the time spent in various MEs across a year. Within a tract, replicates of a given population/subgroup can be run to estimate variability in exposure through sampling of parameter distributions and other stochastic elements of the model. The distribution of estimated exposures for a population/subgroup could be useful in evaluating the relationship between long-term exposures and long-term ambient concentration levels as they relate to the current and any alternative long-term standards that may be under consideration. An additional exposure metric that may be useful is the development of an exposure to ambient concentration ratio, tract-by-tract and location-by-location, to create a distribution of ratios. In locations of interest but not modeled, the ratio can be applied to approximate long-term exposures in these locations, assuming similar population attributes in the extrapolated areas. Comparison of the long-term exposure estimates with potential long-term health effect benchmarks would also be possible however, the 1st draft ISA indicates that the strongest evidence for adverse health conditions is with shorter averaging times. See Section 4 for more detail.

3.4.2.2 Variability and Uncertainty

As described in the Tier II short-term exposure approach (Section 3.4.1), population variability in long-term exposure is better represented by estimating the spatial distribution of ambient concentrations, simulating people and considering their time-location-activity patterns, and addressing moderation of outdoor concentrations to indoor microenvironments. Preserving the time pattern of exposure (the correlation of ME concentrations with peoples' activities) and generating replicates of cohort exposures within tracts serve as additional methods to represent variability.

Limitations to the Tier II long-term exposure approach that would contribute to uncertainty in the exposure estimates are also similar to those described previously for the short-term exposure estimation approach. Although the approach is cohort-based and not person-oriented, and annual average concentrations are used, it is likely that the mean estimates for annual average exposures are reasonable; however, variability in these exposure estimates is likely constrained.

In addition to uncertainties described in Section 3.4.2 regarding limited evaluation of estimated exposure and ME concentrations, some of the uncertainty in this Tier II assessment would be assessed quantitatively through individual parameter analyses and possibly a unified uncertainty analysis as described previously in the recent O_3 NAAQS review (US EPA, 2007e; Langstaff, 2007).

3.5 TIER III: REFINED EXPOSURE ASSESSMENT

Although the above screening-level assessment represents an improvement over the assumption that exposures are equal to ambient concentrations, it relies on a number of simplifying assumptions that still contribute uncertainty to exposure estimates. Depending on the relationship between these screening-level exposure estimates and the exposure-response information, or potential health effect benchmarks for health effects of concern, more refined estimates of exposure may be developed. The purpose of a Tier III exposure assessment would be to refine personal human attributes, such as time-location-activity patterns and human physiology, and to account for factors that may contribute to lessened or greater personal exposures (short- and long-term), including the decay of NO_2 indoors and the relative contribution of indoor sources. The result would be person-based exposure profiles for a given population for durations from one hour to one year.

3.5.1 Approach

The approach would use EPA's Air Pollutants Exposure (APEX) model (US EPA, 2006a; 2006b).[11] APEX is a Monte Carlo simulation model used to simulate a large number of randomly sampled individuals within each urban area reflecting population demographics, thus generating area-wide estimates of population exposure. The PC-based probabilistic model was recently used to estimate population exposures in 12 urban areas for the O_3 NAAQS review (US EPA, 2007e).

Much like HAPEM6, the APEX model simulates exposures in indoor, outdoor, and in-vehicle MEs; however APEX simulations are oriented towards individuals rather than cohorts. The model stochastically generates simulated individuals using census-derived probability distributions from the 2000 census at the census tract level. A national commuting database based on 2000 census data 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.

Like HAPEM6, the APEX model draws human activity data from CHAD (McCurdy et al., 2000), but the data are used to generate longitudinal activity sequences to represent the movement of simulated individuals through time and space, accounting for the effects of particular day-types (e.g., weekday versus weekend) and temperature on daily activities. APEX calculates the concentration in the ME 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.

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

The calculation of ME concentrations in APEX is dependent not only on the parameter distributions for the mass balance and factors approaches, but also on the ambient (outdoor) NO_2 concentrations and temperatures. Surface temperatures will be obtained from the National Weather Service and spatially interpolated for each study area as input to APEX. As described

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

earlier in the Tier II approach, on- and near-roadway ME exposures could be addressed by either one of two different methods and use and/or build upon data developed in the Tier II assessment.

The first method would involve using the modified and interpolated hourly NO_2 concentration measurements derived from the fixed-site monitoring data and emission/dispersion model output. Microenvironmental factors for NO_2 would be needed (starting with those developed above for HAPEM6) and use the general APEX model structure as is for addressing ME concentrations. For the application to NO_2, MEs such as the following would be modeled, depending on available data:

- 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

One principal issue for this tier exposure assessment is to address the population fraction living within the tracts containing major roads and, therefore, the ambient concentrations in these locations. One method could include modifying the APEX model to perform multiple model runs for the same population using the different distance category concentrations as the ambient input (>200m, 75-200m, and <75m) and, post-run, account for the fraction of the population within the given distance category. Note that in-vehicle concentrations would have to be estimated by a model run that uses in-vehicle ME factors to adjust the ambient concentration not under the influence of a major roadway (e.g., adjusting the >200m concentration) or by a model run that uses ME factors that allow for penetration of on-roadway concentrations inside the vehicle. This would require retention of the on-road concentration fields estimated from an emission/dispersion modeling effort, as described in the Tier II short-term exposure (Section 3.4.1). Any additional local sources (e.g., power utilities) could be addressed as well, incorporating dispersion model ambient concentrations within the existing roadway proximity categories, where appropriate. APEX also has the general model structure to address indoor sources, although emission rate estimates, local prevalence, and usage patterns would be required as defined in the Tier II assessment.

A second method, more intensive in terms of model development, would be to develop a module for APEX similar to that in HAPEM6 that addresses the on- and near roadway exposures in the microenvironmental parameters. The fraction of population on and near roadways would be accounted for, as well as more seamlessly addressing on-roadway exposures for both individuals that reside within tracts in close proximity to roadways and those that do not.

3.5.2 Generated Outcomes

Exposure estimates would be generated for current NO_2 levels, for levels assuming just meeting the current NAAQS, and for levels assuming just meeting potential alternative standards. The exposure assessment would take 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 of exposure include counts of people exposed one or more times to a given NO_2 concentration, and counts of person-occurrences of particular exposures. The former counts the number of individuals exposed one or more times per year at the potential EOC (e.g., exposure level at a particular breathing rate). In the case where the exposure estimate is above a potential health effect benchmark, the model estimates the number of people who experience that level of air pollution, or higher, at least once during the modeled period. The person-occurrences measure counts the number of times per year that an individual experiences a potential EOC 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. In addition, annual average exposures can be estimated for each simulated individual, thus the relationship between any long-term and short-term exposure estimates is preserved.

3.5.3 Variability and Uncertainty

The principle objective of a refined exposure assessment would be to estimate exposures by representing the variability in a given population's characteristics that influence its exposure, while minimizing the uncertainties. Variability can be described in terms of the empirical quantities that are important in estimating exposure and are inherently variable across time and space, or when considering a group of individuals (Cullen and Frey, 1999). For example, body mass is a measurable quantity that differs for individuals within a population (depending on a number of factors) and can be represented by frequency distribution(s). Uncertainty tends to reflect the degree of confidence in the use of or the representativeness of models or model components. For example, uncertainties arise in body mass distributions due to random or systematic measurement error, or perhaps uncertainty is introduced by the application of a body mass distribution obtained using one population of individuals to extrapolate to another distinct population of individuals. In this example using a distribution of measured body mass, uncertainty can be present as apparent variability or as unaccounted variability. It is within this general context that variability and uncertainty would be addressed in this tier assessment.

Uncertainty would be assessed quantitatively through individual parameter analyses and possibly a unified uncertainty analysis as described previously in the recent O_3 NAAQS review (US EPA, 2007e; Langstaff, 2007). Briefly, there are two primary sources of uncertainty that would be addressed in this type of a quantitative analysis. The first is uncertainty associated with the model inputs (e.g., use of air quality data, time-location-activity diaries, microenvironmental factor distributions). The second is uncertainty associated with model formulation (e.g., algorithms included in the model).

In the case of model inputs, information is often available to characterize variability, and on occasion, both variability and uncertainty. APEX is a Monte Carlo simulation model that explicitly incorporates the variability inherent in the model input data. A 2-dimensional Monte Carlo Latin hypercube sampling approach could be used to provide a combined variability and uncertainty analysis for APEX. A Monte Carlo approach entails performing a large number of model runs with inputs randomly sampled from specified distributions that reflect the variability and uncertainty of the model inputs. The 2-dimensional Monte Carlo method allows for the separate characterization of variability and uncertainty in the model results (Morgan and Henrion, 1990). If this approach were taken, developing appropriate distributions representing both variability and uncertainty in model inputs (e.g., air exchange rates, NO_2 decay rates, physiological parameters) would be a key part of the effort.

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

3.6 CRITERIA FOR DETERMINING APPROACH

Criteria have been developed to determine the Tier level of the assessment to be performed. The criteria are designed to determine the value added to the assessment as indicated by assumptions retained in each tier and the potential reduction of uncertainties in the exposure estimates (Figure 5). The general factors identified below will be considered in the progression from one Tier to each subsequent Tier.

- Outcome of the ambient air quality analysis, including the estimated number of peak concentrations using current ambient concentrations and those assuming any potential alternative standards that may be under consideration.
- Availability of information and data defining the potential impact of roadway NO_2 concentrations and other important local sources on nearby residents and on specific microenvironmental concentrations (e.g., while traveling inside motor vehicles).
- Existence of the data required to perform the analyses in each subsequent Tier of the assessment
- Representation of identified susceptible populations in the current review.

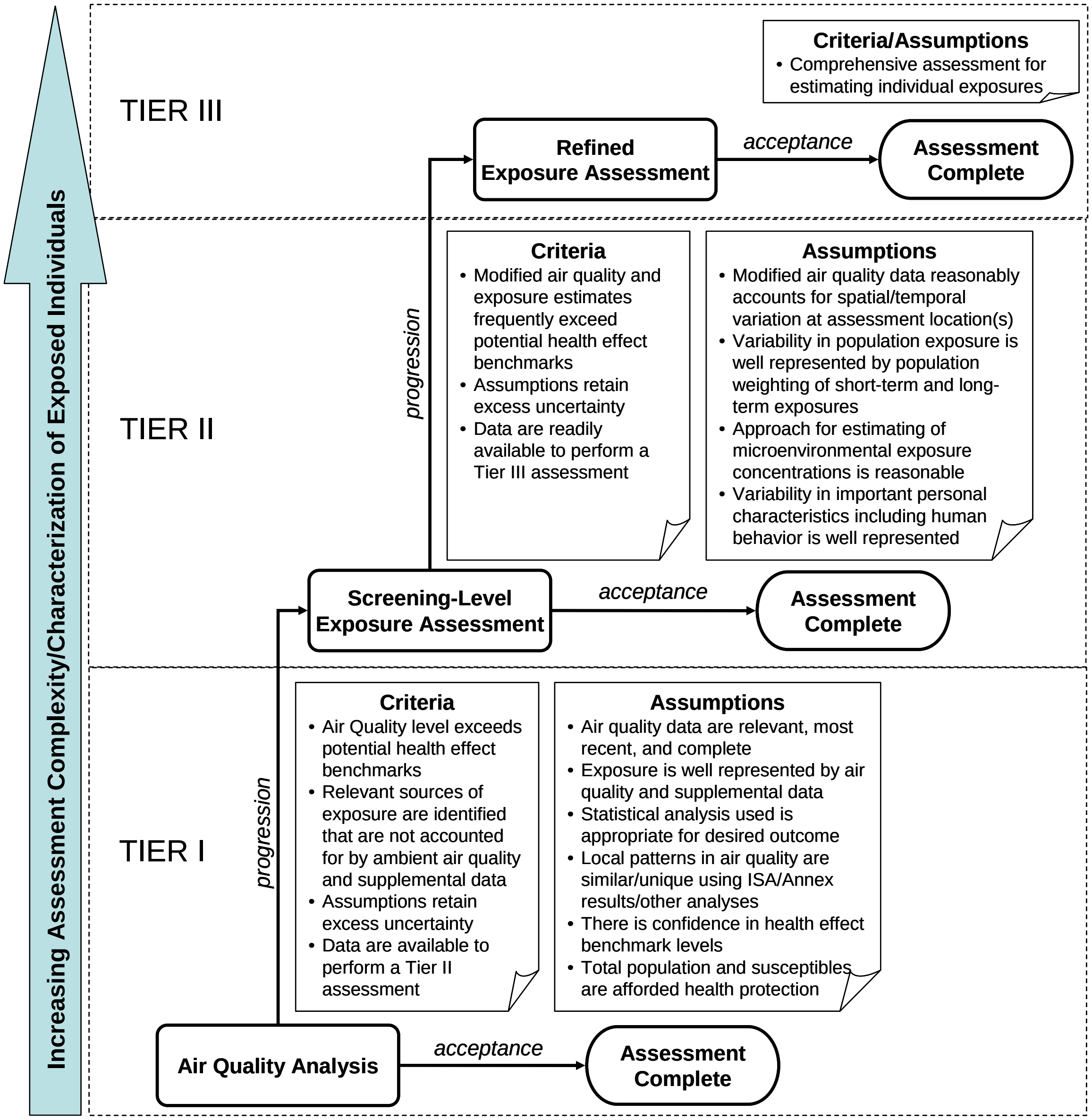

Figure 5. Illustration of the Criteria Associated with Progression through Tiered Exposure Assessment and Basic Assumptions for Tier Acceptance.

4. RISK ASSESSMENT SCOPE AND METHODS

4.1 OVERVIEW

A two-tiered approach to characterizing health risks will be employed. In a first tier analysis, potential health effect benchmarks based on information in the draft ISA will be combined with air quality (serving as a surrogate for exposure) or exposure estimates from the exposure assessment to characterize population health risks. A second tier risk assessment, if conducted, will involve combining concentration-response (C-R) and/or exposure-response (E-R) data with either ambient air concentration distributions or exposure concentration distributions, respectively to generate population risk estimates for one or more health endpoints. Whether a Tier II risk assessment is conducted will depend on the availability of data and on the anticipated utility of results to inform decisions on the adequacy of the NO_2 NAAQS. In addition to the Tier I and Tier II quantitative assessments that may be conducted, the health risk/exposure assessment document will include a qualitative discussion of significant health endpoints to provide a broader public health context.

The methods used to conduct the risk assessment, as well as the summary results and discussion of key findings from the assessment will be presented in the first draft of the health risk/exposure assessment document. This document will focus on risks associated with recent NO_2 levels and historical NO_2 levels representing just meeting the current annual NO_2 standard. The second draft health risk/exposure assessment document will include estimates and discussion of key findings associated with just meeting any potential alternative NO_2 standards that may be considered.

The goals of the NO_2 risk assessment are: (1) to estimate the number of occurrences of short-term air quality events at or above potential health effect benchmarks associated with recent air quality levels and air quality levels just meeting the current and potential alternative NO_2 standards, (2) to estimate the number of people exposed at or above potential health effect benchmarks associated with recent air quality levels and air quality levels just meeting the current and potential alternative NO_2 standards, (3) to provide distributions of population health risk estimates for selected health endpoints associated with recent NO_2 air quality levels and air quality levels just meeting the current and potential alternative NO_2 standards if a Tier II risk assessment is conducted, and (4) to identify and discuss key assumptions, degree of variability, and nature and extent of uncertainties in the estimates, and (5) to characterize quantitatively, where feasible, the uncertainties and variability in the estimates.

Conceptually, if there were sufficient scientific data available, the objective of the health risk assessment portion of the analysis would be to develop population-based health risks for various health effect endpoints in at-risk population groups associated with recent air quality levels and just meeting the current and potential alternative NO_2 NAAQS. In addition, the health risk assessment would include a quantitative characterization of the uncertainties in those risk estimates and key assumptions underlying such estimates. We recognize that the current state-of-knowledge about NO_2-related health effects, as reflected in the evaluation contained in the 1^{st}

draft ISA, likely precludes the development of quantitative health risk estimates for most health endpoints discussed in the ISA. Our initial judgments about health effect categories and appropriate approaches to conduct the assessments are presented below and are based on the 1st draft ISA, recognizing that the 1st draft risk assessment will be informed by CASAC and public review of the 1st draft ISA and the information and evaluation contained in the 2nd draft ISA and relevant Annexes.

The 1st draft ISA indicates that the strongest health findings are for adverse respiratory effects and that the exposure indices associated with these effects are typically for one-hour and 24-hour averaging times. The approach for characterizing the risks associated with short-term health effects associated with these short-term exposure durations are discussed in the next section. The health evidence related to long-term exposure to NO_2 ranges from suggestive to inconclusive for effects ranging from respiratory morbidity to mortality. Therefore, based on our review of the 1st draft ISA, we do not anticipate developing risk estimates for NO_2-related effects associated with long-term NO_2 exposures.

4.2 TIER I: HEALTH EFFECT BENCHMARKS

This type of risk characterization will initially use air quality estimates, along with a range of potential health effect benchmarks that will be identified based on information in the 2nd draft ISA and relevant Annexes, to estimate the number of occurrences at or above levels that are likely to cause adverse health effects in some members of the identified at-risk population groups. Multiple air quality scenarios will be analyzed, including recent ambient air quality levels enhanced by including local source contributions, historical air quality levels when air quality was at or near the level of the current annual NO_2 standard, and air quality levels associated with just meeting any potential alternative NO_2 standards that may be considered.

4.2.1 Approach

For the purposes of this assessment, the approach is similar to calculating a hazard quotient, which is the ratio of the air quality concentration or exposure concentration (either population-weighted or individual exposure depending on the Tier assessment output) to the potential health effect benchmark concentration. Counts would be obtained for the number of times the various potential health effect benchmarks are exceeded. We envision analyzing several potential health effect benchmark levels.

The first step is to identify key studies outlined in the ISA and Annexes that provide evidence for a specific adverse health effect and the associated averaging time. This includes analyses indicating effects attributed to NO_2 exposure alone as well as where potential effects of air pollutant confounders (e.g., O_3 or PM) have been removed. Controlled human exposure studies have measured short-term health effects related to specific NO_2 exposures, such as airway responsiveness to allergen and non-specific challenges. The lowest exposure levels of concern generally ranged from 0.2 to 0.3 ppm for short-term exposures of differing duration (ranging from 15-minutes to 2-hours), with asthmatics identified as being much more susceptible to NO_2 exposure than healthy individuals. Health effects were not seen in healthy persons at any NO_2 concentration less than <1 ppm (1-hr averaging time) in controlled human exposure studies, a level well above current ambient concentrations and exposure concentrations measured in the presence of local source emissions. Based on the current evaluation in the 1st draft ISA, we have tentatively identified potential health effect benchmarks in the range of 0.2 to 0.3 ppm (1-hr averaging time) for use in the Tier I risk assessment. We also have identified asthmatics (children and adults) as the population groups most at-risk from respiratory-related effects associated with these benchmark levels.

4.2.2 Generated Outcomes

Depending on the tier of the exposure assessment performed, generated outcomes could be the number of occurrences that air quality exceeds a potential health effects benchmark, as well as the number of times a population or an individual experiences an exposure of concern in a given year, considering recent air quality levels and air quality levels just meeting the current NO_2 standard and any potential alternative NO_2 standards that may be considered. Frequencies would be given for each population subgroup analyzed and the particular locations of interest.

4.2.3 Variability and Uncertainty

Variability in the context of the Tier I risk assessment can be described in terms of the empirical quantities and relationships that are important in estimating health risks and are inherently variable across time and space, or when considering a group of individuals (Cullen and Frey, 1999). For the initial Tier I screening level assessment that estimates the number of exceedances of alternative potential health effect benchmarks across several example urban areas selected for the assessment, results for the individual locations incorporate and illustrate the variability due to differences in air quality patterns and distributions. If a Tier II or III exposure assessment is conducted, then a second phase of the Tier I level risk assessment would generate estimates of the number of people exposed to levels at or above the various potential health effect benchmark levels. Results for the individual urban areas included in this assessment would incorporate and reflect the variability in air quality and the variability in key inputs that impact estimation of population exposure including, but not limited to, the spatial pattern of the population, activity patterns, air exchange rates, proximity to roadways, and presence of indoor sources.

Consistent with the approach described above in Section 3, a tiered approach to assessing uncertainty will be employed with the goal of progressing to a quantitative analysis if warranted and if data are available to support such an analysis. The first step in the uncertainty analysis would be to identify the components of the assessment that do or do not contribute to uncertainty, and provide a rationale for why this is the case. Section 3.3.3 above provides a preliminary qualitative evaluation for the uncertain components of the planned Tier I air quality analysis and exposure assessment, indicating the direction of influence (under- or over-estimate) on air quality and exposure estimates that would be used in the Tier I health risk assessment.

In addition to uncertainties related to the air quality analysis and/or exposure assessment components of a Tier I risk assessment, there is uncertainty related to the potential health effect benchmark levels used in the assessment. The use of any specific potential health effect benchmark assumes that the level is appropriate for application to all susceptible individuals equally, between and within each population subgroup. Recognizing that there is both considerable variability in responsiveness and uncertainty associated with the use of any single potential health effect benchmark, a range of potential health effect benchmarks will be included in the Tier I assessments, allowing the decision maker to gain some insight into the impact that uncertainty about the level at which adverse health effects are likely to occur has on the Tier I estimates. From a directional perspective, we have greater confidence that higher potential health effect benchmarks are associated with susceptible individuals being adversely affected and that a larger fraction of the population is likely to experience adverse health effects. Conversely, we have less confidence that adverse health effects will occur at lower benchmark levels and a smaller fraction of the population is likely to experience adverse health effects.

4.3 TIER II: RISK BASED ON EPIDEMIOLOGICAL STUDIES

As noted above, based on review of the scientific evidence from controlled human exposure studies, there is not sufficient information to develop credible exposure-response relationships for NO_2-related respiratory health effects for use in a quantitative risk assessment. In contrast, epidemiological studies do provide estimated C-R relationships based on data collected in environmentally-relevant settings. Ambient NO_2 concentration is typically measured as the average of monitor-specific measurements, although personal exposures are occasionally measured. Health responses reported to be related to NO_2 include, but are not limited to, respiratory symptoms in asthmatic children, asthma emergency department visits, and respiratory related hospital admissions. As described more fully below, a risk assessment based on epidemiological studies typically requires baseline incidence rates for the specific health endpoints and population data for the specific risk assessment locations.

4.3.1 Approach

As noted earlier in this plan, previous reviews of the NO_2 primary NAAQS completed in 1985 and 1994 did not include quantitative health risk assessments. Thus, the planned risk assessment described in this Scope and Methods Plan builds upon the methodology and lessons learned from the risk assessment work conducted for the recent PM and current O_3 NAAQS reviews (Abt Associates, 2005; Abt Associates, 2007). Many of the same methodological issues are present for each of these criteria air pollutants where epidemiological studies provided the basis for the C-R relationships used in the quantitative risk assessment. The plans discussed below are based on the information and evaluation contained in the 1st draft ISA and some aspects of these plans may change based on CASAC and public comments on the 1st draft ISA and changes that will be incorporated in the 2nd draft ISA. The discussion below represents current staff thinking with respect to health effect endpoints that are candidates for including in a Tier II risk assessment and those health endpoints for which there is insufficient evidence to consider including in a quantitative risk assessment.

4.3.1.1 Selection of Health Effect Endpoints

In selecting potential health endpoints to include in a Tier II risk assessment, we plan to focus on health endpoints that have well-defined health consequences (i.e., where there is consensus about the degree of response that represents an adverse health effect). In addition, we are focusing on health endpoint categories identified in the ISA where the weight of evidence supports the inference of a likely causal relationship. As discussed below, once we identify candidate health endpoints based on these criteria, there are additional factors that must be considered in deciding whether to proceed with a quantitative Tier II risk assessment. These include: (1) the likely utility of such information in the decision, (2) the availability of sufficient C-R data that is relevant to locations in the U.S., and (3) the availability of baseline incidence data for the health effects to be analyzed.

As discussed in the 1st draft of the ISA and associated Annex covering epidemiological studies, there are several epidemiological and field studies examining a variety of health effects associated with ambient NO_2 concentrations in locations throughout the U.S., Canada, Europe, and other regions of the world that have been published since the last NO_2 NAAQS review. The 1st draft ISA concludes that recent studies provide strong scientific evidence that NO_2 is associated with a range of respiratory effects and describe a likely causal relationship between short-term NO_2 exposure and adverse effects on the respiratory system. The draft ISA concludes that the strongest epidemiological evidence exists for associations with increased emergency department visits and hospital admissions for respiratory causes, especially asthma and COPD, with short-term (typically 1- and 24-hr average) ambient concentrations of NO_2. In contrast, the 1st draft ISA concludes that the overall evidence is inconclusive regarding the effect of short-term exposures to NO_2 on the cardiovascular system. The 1st draft ISA concludes that the epidemiological evidence is suggestive of associations between short-term exposures to NO_2 and non-accidental and cardiopulmonary-related mortality but notes the limited experimental evidence to support judgments about biological plausibility and raises concerns about whether NO_2 is acting as a marker for other pollutants, including PM and SO_2, or as a marker for traffic-related mixtures. The 1st draft ISA also concludes that the evidence is inconclusive regarding the association between long-term exposure to NO_2 and mortality.

Based on the evaluation of the health effects evidence in the 1st draft ISA, the following health effect endpoints are judged to be the most appropriate candidates for developing quantitative risk estimates:

- Respiratory-related hospital admissions, especially for asthmatics
- Respiratory-related emergency department visits, especially for asthmatic children
- Respiratory symptoms (e.g., cough, wheeze), particularly in children and asthmatics.

Generally, for a Tier II quantitative risk assessment based on C-R relationships derived from epidemiological studies, it is preferable to use C-R relationships based on studies that were conducted in the same location chosen for the risk assessment. Using C-R relationships from studies conducted in locations different than the risk assessment locations introduces additional uncertainty into the risk assessment due to potential differences in population, air quality patterns, exposure patterns, and other factors that may have influenced the relationship between exposure to the pollutant of interest and the health effect outcome. It should be noted that many of the epidemiological studies for the three health endpoints identified above were conducted in Canada, Europe, Asia, and other locations outside of the United States. For some of these health endpoints, the effect estimates were more consistently positive and statistically significant in European studies than those conducted in the U.S. Following review of the 1st draft ISA and considering any comments and recommendations by CASAC and the public, we plan to evaluate whether the existing epidemiological studies provide C-R relationships that are judged suitable for applying in selected U.S. urban locations. In addition, we are in the process of evaluating whether we can obtain baseline incidence data for emergency department visits and respiratory-related hospital admissions for candidate U.S. urban locations that would be included in a Tier II risk assessment.

4.3.1.2 Selection of Concentration-Response Functions

If a Tier II risk assessment is judged to be both feasible and of sufficient utility, then appropriate C-R relationships will have to be selected for inclusion in the assessment. Studies often report more than one estimated C-R function for the same location and health endpoint. Sometimes models include different sets of co-pollutants and/or different time lags. For some health endpoints, there are studies that estimated multi-city NO_2 C-R functions, while other studies estimated single-city functions.

As noted above, all else being equal, staff judges that a C-R function estimated in the assessment location is preferable to a function estimated in some other location, to avoid any 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 effect coefficient. Because single-city and multi-city studies have different advantages, staff plans to include both types of functions, where they are available.

Most NO_2 epidemiological studies include C-R functions in which NO_2 was the only pollutant entered in the model as well as other C-R functions in which NO_2 and one or more co-pollutants (e.g., PM, SO_2, CO, O_3) 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 NO_2 in single pollutant models, risks attributed to NO_2 might be overestimated where C-R functions are based on single pollutant models. However, if co-pollutants are highly correlated with NO_2, their inclusion in an NO_2 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 NO_2 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, if a Tier II risk assessment is developed, staff plans to report risk estimates based on both types of models, where both are available.

4.3.1.3 Baseline Health Effects Incidence Considerations

The most common epidemiological-based health risk model expresses the reductions in health risk (Δy) associated with a given reduction in NO_2 concentrations (Δx) as a percentage of the baseline incidence (y). Thus, information on the baseline incidence of health effects (i.e., the incidence under "as is" air quality conditions) in each location is needed. Where at all possible, staff plans to use county-specific incidences or incidence rates (in combination with county-specific population data). Staff is investigating whether recent baseline incidence data is available for respiratory-related emergency department visits and respiratory-related hospital admissions for potential assessment locations.

For respiratory symptoms, there may be no information on baseline incidence other than that reported in the original epidemiological study. We recognize that lack of recent location-specific incidence data will increase the uncertainty surrounding any risk estimates that may be generated in a Tier II risk assessment.

4.3.2 Generated Outcomes

If a Tier II risk assessment is conducted, both central tendency and 95% confidence interval estimates would be provided and such estimates would be expressed using several risk metrics. These risk metrics would include the estimated incidence (i.e., number of cases), percent of total incidence, and incidence per 100,000 relevant population for each health endpoint and location included in the assessment. Results would also be presented for the reduction in incidence and percent reduction associated with moving from air quality just meeting the current standard to air quality just meeting any potential alternative standards identified for consideration. Staff recognizes that any such projected reductions would be hypothetical reductions because all urban areas with current NO_2 ambient monitors have recent NO_2 levels that are notably below the current annual NO_2 standard.

4.3.3 Variability and Uncertainty

There are several uncertainties that affect the inputs to any Tier II NO_2 risk assessment based on C-R functions derived from epidemiological studies. These include uncertainties in the procedures used to simulate just meeting potential alternative NO_2 standards, baseline incidence rates, and appropriate model form for the C-R relationships used in a risk assessment. There also is city-to-city variability in C-R relationships due to variability in air quality and exposure patterns and population differences. Presentation of separate risk results for selected example urban areas would incorporate and reflect variability in several key inputs to the health risk assessment (e.g., variability in air quality patterns and baseline incidence data).

Consistent with the approach used in the recent O_3 and PM NAAQS risk assessments, the uncertainty resulting from the statistical uncertainty associated with the estimate of the NO_2 health effect coefficient in the C-R function can be characterized by confidence intervals around the corresponding point estimates of risk. However, these confidence intervals only address sampling error and do not address broader uncertainties concerning the overall shape or form of the C-R relationships. As noted above, if a Tier II assessment is conducted, Staff plans to include results using both single- and multi-city models, and single- and multi-pollutant models and C-R functions based on different epidemiological studies. Presentation of a range of results would provide decision makers with some perspective on the impact of alternative models and the degree of uncertainty associated with any risk estimates.

4.4 CRITERIA FOR DETERMINING APPROACH

The factors identified below will be considered in deciding whether to conduct a Tier II quantitative risk assessment.

- Outcome of the Tier I risk assessment with respect to the magnitude and the degree of uncertainty in the estimated number of concentrations and/or exposures exceeding several potential health effect benchmark levels associated with current ambient concentrations and with NO_2 levels just meeting the current and any potential alternative standards that may be considered.
- Availability of information and data required to conduct a Tier II risk assessment, including baseline incidence data and C-R relationships that are judged suitable for applying in several example U.S. urban areas.
- The utility or value-added to the decision process of a Tier II risk assessment, beyond that provided by the Tier I assessment. For example, is a Tier II risk assessment likely to reduce or better characterize uncertainties in the characterization of NO_2-related health risks compared to that of a Tier I assessment.
- The feasibility of conducting a credible Tier II risk assessment within the consent decree schedule and available resources.

4.5 BROADER HEALTH RISK CHARACTERIZATION

The exposure/health risk assessment document will include both summary air quality information for the U.S. and summary information and discussion of the various health effects identified in the 2nd draft ISA to help provide a broad context for the quantitative risk estimates that are provided in the Tier I and/or Tier II risk assessments. Thus, air quality statistics for all areas with NO_2 monitoring data will be presented, to put into perspective the results of the assessment involving the selected urban areas included in the quantitative assessment. National scale information on the size of various at-risk populations also will be presented.

5. SCHEDULE AND MILESTONES

Table 5 lists the key milestones for the risk/exposure assessment that will be conducted as part of the current NO_2 NAAQS review. Consultation with the CASAC NO_x/SO_x Panel is planned for October 26, 2007 to obtain input on this draft Scope and Methods Plan. Staff will then proceed to develop exposure and health risk estimates associated with recent NO_2 ambient concentrations, levels representing just meeting the current NO_2 standard, and potential alternative standards. These estimates and the methodology used will be presented in the first draft NO_2 risk/exposure assessment and technical support documents. The draft report will be released for CASAC and public review in March 2008. EPA will receive comments on these draft documents from the CASAC NO_2 Panel and general public at a meeting in May 2008. A revised assessment will be released in September 2008 for review by CASAC and public at a meeting to be held in November 2008. Staff will consider these review comments and prepare a final risk/exposure assessment by January 2009.

Table 5. Key Milestones for the Exposure and Health Risk Assessment for the NO_2 NAAQS Review.

Milestone	Date
Release 1st draft NO_2 ISA	August 2007
Release 1st draft NO_2 Risk/Exposure Scope and Methods Plan	September 2007
CASAC/public review and meeting on 1st draft NO_2 ISA	October 24-25, 2007
CASAC consultation on 1st draft NO_2 Risk/Exposure Scope and Methods Plan	October 25, 2007
Release 2nd draft NO_2 ISA	February 2008
Release 1st draft of the NO_2 Risk/Exposure Assessment	March 2008
CASAC/public review and meeting on 2nd draft NO_2 ISA and 1st draft of the Risk/Exposure Assessment	May 2008
Final NO_2 ISA	July 2008
Release 2nd draft of the NO_2 Risk/Exposure Assessment	September 2008
CASAC/public review and meeting on 2nd draft of the NO_2 Risk/Exposure Assessment	November 2008
Final NO_2 Risk/Exposure Assessment	January 2009

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