Risk and Exposure Assessment to Support the Review of the NO_2 Primary National Ambient Air Quality Standard: Second Draft

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This draft document 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 draft document should be addressed to Scott Jenkins, U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, C504-06, Research Triangle Park, North Carolina 27711 (email: Jenkins.scott@epa.gov).

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List of Acronyms/Abbreviations

AADT	Annual average daily traffic
A/C	Air conditioning
AER	Air exchange rate
AERMOD	American Meteorological Society (AMS)/EPA Regulatory Model
AHS	American Housing Survey
APEX	EPA's Air Pollutants Exposure model, version 4
ANOVA	One-way analysis of variance
AQS	EPA's Air Quality System
AS	Asthma symptoms
BRFSS	Behavioral Risk Factor Surveillance System
C	Cough
CAA	Clean Air Act
CAMD	EPA's Clean Air Markets Division
CASAC	Clean Air Scientific Advisory Committee
CDC	Centers for Disease Control
CHAD	EPA's Consolidated Human Activity Database
CHF	Congestive Heart Failure
Clev/Cinn	Cleveland and Cincinnati, Ohio
CMSA	Consolidated metropolitan statistical area
CO	Carbon monoxide
COPD	Chonic Obstructive Pulmonary Disease
COV	Coefficient of Variation
C-R	Concentration-Response
CTPP	Census Transportation Planning Package
DVRPC	Delaware Valley Regional Planning Council
EDR	Emergency department visits for respiratory disease
EDA	Emergency department visits for asthma
EDAC	Emergency department visits for asthma – children
HAAC	Hospital admissions for asthma - children
ER	Emergency room
EPA	United States Environmental Protection Agency
EOC	Exposure of Concern
GM	Geometric mean
GSD	Geometric standard deviation
GST	Glutathione *S*-transferase (e.g., GSTM1, GSTP1, GSTT1)
h	Hour
HNO3	Nitric acid
HONO	Nitrous acid
ID	Identification
ISA	Integrated Science Assessment
ISH	Integrated Surface Hourly Database
km	Kilometer

L95	Lower limit of the 95th confidence interval
LA	Los Angeles, California
m	Meter
max	Maximum
ME	Microenvironment
med	Median
MI	Myocardial Infarction
min	Minimum
MSA	Metropolitan statistical area
NAAQS	National Ambient Air Quality Standards
NAICS	North American Industrial Classification System
NCEA	National Center for Environmental Assessment
NEI	National Emissions Inventory
NEM	NAAQS Exposure Model
NCDC	National Climatic Data Center
NHAPS	National Human Activity Pattern Study
NHIS	National Health Interview Survey
NO_2	Nitrogen dioxide
NO_x	Oxides of nitrogen
NO_3^-	Nitrate ion
NWS	National Weather Service
NYC	New York City
NYDOH	New York Department of Health
O_3	Ozone
OAQPS	Office of Air Quality Planning and Standards
OR	Odds ratio
ORD	Office of Research and Development
ORIS	Office of Regulatory Information Systems identification code
POC	Parameter occurrence code
ppb	Parts per billion
PEN	Penetration factor
PM	Particulate matter
ppm	Parts per million
PRB	Policy-Relevant Background
PROX	Proximity factor
PVMRM	Plume Volume Molar Ratio Method
RECS	Residential Energy Consumption Survey
RIU	Rescue inhaler use
RR	Relative risk
SAS	Statistical Analysis Software
SB	Shortness of breath
SEP	Social-economic position
SIC	Standard Industrial Code
SD	Standard deviation
se	Standard error
TDM	Travel Demand Modeling

tpy	Tons per year
TRIM	EPA's Total Risk Integrated Methodology
U95	Upper limit of the 95th confidence interval
US DOT	United States Department of Transportation
US EPA	United States Environmental Protection Agency
USGS	United States Geological Survey
VMT	Vehicle miles traveled
W	Wheeze

1. INTRODUCTION

1.1 OVERVIEW

The U.S. Environmental Protection Agency (EPA) is 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 (The Act) govern the establishment and periodic review of the air quality criteria and the NAAQS. These standards are established for pollutants that may reasonably be anticipated to endanger public health or welfare, and whose presence in the ambient air results from numerous or diverse mobile or stationary sources. The NAAQS are based on air quality criteria, which reflect the latest scientific knowledge useful in indicating the kind and extent of identifiable effects on public health or welfare that may be expected from the presence of the pollutant in ambient air. The EPA Administrator promulgates and periodically reviews primary (health-based) and secondary (welfare-based) NAAQS for such pollutants. Based on periodic reviews of the air quality criteria and standards, the Administrator makes revisions in the criteria and standards and promulgates 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).

The Agency has recently made a number of changes to the process for reviewing the NAAQS (described at http://www.epa.gov/ttn/naaqs/). In making these changes, the Agency consulted with CASAC. This new process, which is being applied to the current review of the NO_2 NAAQS, contains four major components. Each of these components, as they relate to the review of the NO_2 primary NAAQS, is described below.

The first of these components is an integrated review plan. This plan presents the schedule for the review, the process for conducting the review, and the key policy-relevant science issues that will guide the review. The integrated review plan for this review of the NO_2 primary NAAQS is presented in the *Integrated Review Plan for the Primary National Ambient Air Quality Standard for Nitrogen Dioxide* (EPA, 2007a). The policy-relevant questions identified in this document to guide the review are:

- Has new information altered the scientific support for the occurrence of health effects following short- and/or long-term exposure to levels of nitrogen oxides (NO_x) found in the ambient air?
- What do recent studies focused on the near-roadway environment tell us about health effects of NO_x?
- At what levels of NO_x exposure do health effects of concern occur?
- Has new information altered conclusions from previous reviews regarding the plausibility of adverse health effects caused by NO_x exposure?
- To what extent have important uncertainties identified in the last review been reduced and/or have new uncertainties emerged?
- What are the air quality relationships between short-term and long-term exposures to NO_x?

Additional questions will become relevant if the evidence suggests that revision of the current standard might be appropriate. These questions are:

- Is there evidence for the occurrence of adverse health effects at levels of NO_x lower than those observed previously? If so, at what levels and what are the important uncertainties associated with that evidence?
- Do exposure estimates suggest that exposures of concern for NO_x-induced health effects will occur with current ambient levels of NO_2 or with levels that just meet current, or potential alternative, standards? If so, are these exposures of sufficient magnitude such that the health effects might reasonably be judged to be important from a public health perspective? What are the important uncertainties associated with these exposure estimates?
- Do the evidence, the air quality assessment, and the risk/exposure assessment provide support for considering different standard indicators or averaging times?
- What range of levels is supported by the evidence, the air quality assessment, and the risk/exposure assessments? What are the uncertainties and limitations in the evidence and the assessments?

- What is the range of forms supported by the evidence, the air quality assessment, and the exposure/risk assessments? What are the uncertainties and limitations in the evidence and the assessments?

The second component of the review process is a science assessment. A concise synthesis of the most policy-relevant science has been compiled into the Integrated Science Assessment (ISA). The ISA is supported by a series of annexes that contain more detailed information about the scientific literature. The ISA to support this review of the NO_2 primary NAAQS is presented in the *Integrated Science Assessment for Oxides of Nitrogen - Health Criteria*, henceforth referred to as the ISA (EPA, 2008a).

The third component of the review process is a risk and exposure assessment, the second draft of which is described in this document. The purpose of this draft document is to communicate EPA's assessment of exposures and risks associated with ambient NO_2. This second draft of the risk and exposure assessment develops estimates of human exposures and risks associated with current ambient levels of NO_2, with levels that just meet the current standard, and with levels that just meet potential alternative standards. Figure 1-1 (below) presents a schematic overview of the analyses described in this document and how those analyses fit together. Each of the steps highlighted in Figure 1-1 is described in more detail in subsequent sections of this document.

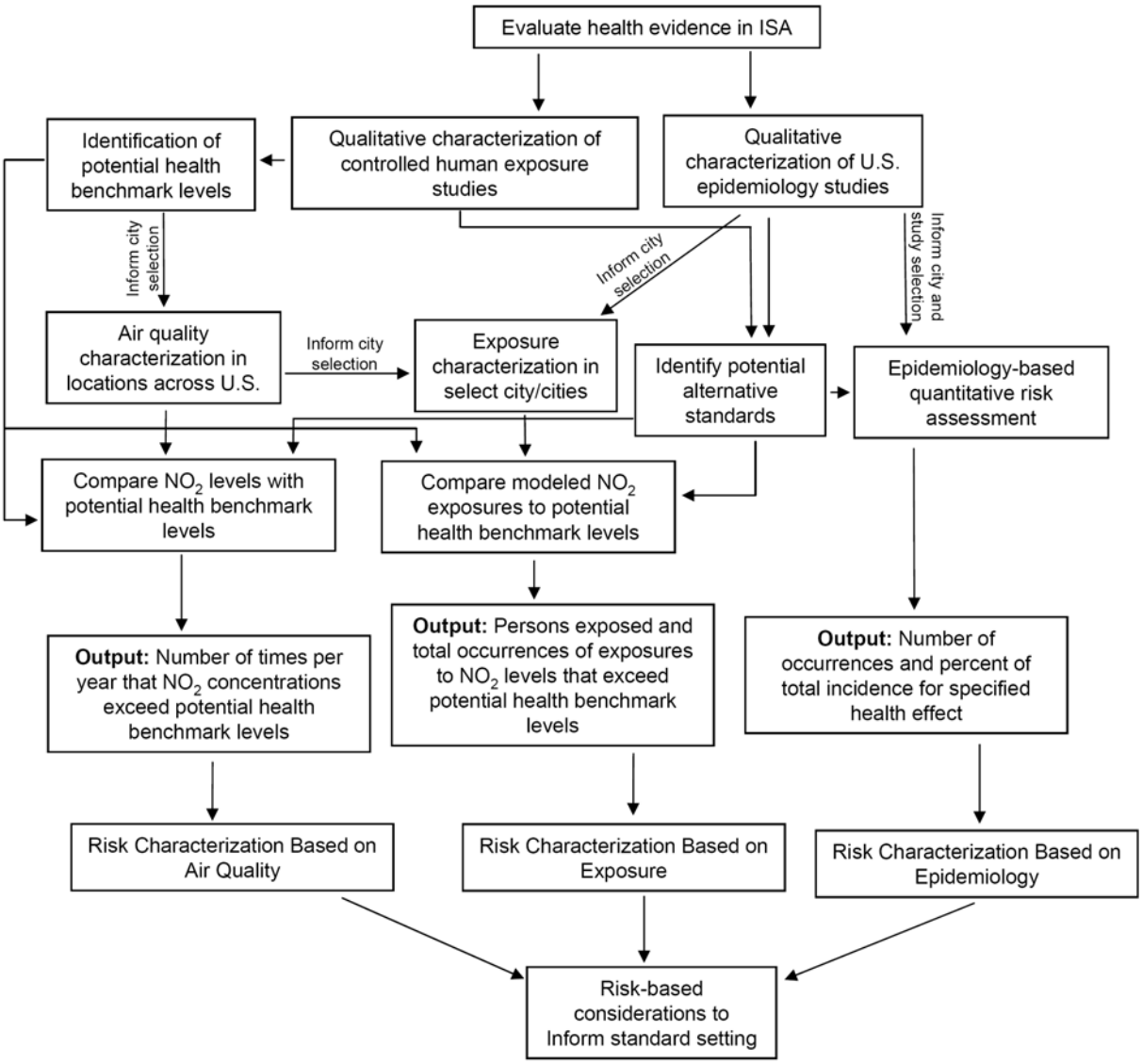


Figure 1-1. Overview of the analyses described in this document and their interconnections

The results of the risk and exposure assessment will be considered alongside the health evidence, as evaluated in the final ISA, to inform the policy assessment and rulemaking process (see below). The draft plan for conducting the risk and exposure assessment to support the NO_2 primary NAAQS is presented in the *Nitrogen Dioxide Health Assessment Plan: Scope and Methods for Exposure and Risk Assessment*, henceforth referred to as the Health Assessment Plan (EPA, 2007b). The first draft of the risk and exposure assessment is presented in *Risk and Exposure Assessment to Support the Review of the NO_2 Primary National Ambient Air Quality Standard: First Draft* (EPA, 2008b).

The fourth component of the process is the policy assessment and rulemaking. The Agency's views on policy options will be published in the Federal Register as an advance notice of proposed rulemaking (ANPR). This policy assessment will address the adequacy of the current standard and of any potential alternative standards, which will be defined in terms of indicator, averaging time, form,[1] and level. To accomplish this, the policy assessment will consider the results of the final risk and exposure assessment as well as the scientific evidence (including evidence from the epidemiologic, controlled human exposure, and animal toxicological literatures) evaluated in the ISA. Taking into consideration CASAC advice and recommendations, as well as public comment on the ANPR, the Agency will publish a proposed rule, to be followed by a public comment period. Taking into account comments received on the proposed rule, the Agency will issue a final rule to complete the rulemaking process.

1.2 HISTORY

1.2.1 History of the NO_2 NAAQS

On April 30, 1971, EPA promulgated identical primary and secondary NAAQS for NO_2 under section 109 of the Act. The standards were set at 0.053 parts per million (ppm), annual average (36 FR 8186). In 1982, EPA published *Air Quality Criteria for Oxides of Nitrogen* (EPA, 1982), which updated the scientific criteria upon which the initial NO_2 standards were based. On February 23, 1984, EPA proposed to retain these standards (49 FR 6866). After taking into account public comments, EPA published the final decision to retain these standards on June 19, 1985 (50 FR 25532).

On July 22, 1987, EPA announced that it was undertaking plans to revise the 1982 air quality criteria (52 FR 27580). In November 1991, EPA released an updated draft air quality criteria document for CASAC and public review and comment (56 FR 59285). The draft document provided a comprehensive assessment of the available scientific and technical information on health and welfare effects associated with NO_2 and other oxides of nitrogen. The CASAC reviewed the draft document at a meeting held on July 1, 1993 and concluded in a closure letter to the Administrator that the document "provides a scientifically balanced and defensible summary of current knowledge of the effects of this pollutant and provides an

[1] The "form" of a standard defines the air quality statistic that is to be compared to the level of the standard in determining whether an area attains the standard.

adequate basis for EPA to make a decision as to the appropriate NAAQS for NO_2" (Wolff, 1993). The Air Quality Criteria Document for the Oxides of Nitrogen was then finalized (EPA, 1993).

The EPA also prepared a Staff Paper that summarized an air quality assessment for NO_2 conducted by the Agency (McCurdy, 1994), summarized and integrated the key studies and scientific evidence contained in the revised air quality criteria document, and identified the critical elements to be considered in the review of the NO_2 NAAQS. The CASAC reviewed two drafts of the Staff Paper and concluded in a closure letter to the Administrator (Wolff, 1995) that the document provided a "scientifically adequate basis for regulatory decisions on nitrogen dioxide." In September of 1995, EPA finalized the Staff Paper entitled, "Review of the National Ambient Air Quality Standards for Nitrogen Dioxide: Assessment of Scientific and Technical Information" (EPA, 1995).

In October 1995, the Administrator announced her proposed decision not to revise either the primary or secondary NAAQS for NO_2 (60 FR 52874; October 11, 1995). A year later, the Administrator made a final determination not to revise the NAAQS for NO_2 after careful evaluation of the comments received on the proposal (61 FR 52852, October 8, 1996). The level for both the existing primary and secondary NAAQS for NO_2 is 0.053 parts per million (ppm) (100 micrograms per cubic meter of air [$\mu g/m^3$]), annual arithmetic average, calculated as the arithmetic mean of the 1-hour NO_2 concentrations.

1.2.2 Health Evidence from Previous Review

The prior Air Quality Criteria Document (AQCD) for Oxides of Nitrogen (EPA, 1993) concluded that there were two key health effects of greatest concern at ambient or near-ambient levels of NO_2, increased airway responsiveness in asthmatic individuals after short-term exposures and increased occurrence of respiratory illness in children with longer-term exposures. Evidence also was found for increased risk of emphysema, but this was of major concern only with exposures to levels of NO_2 much higher than then-current ambient levels. The evidence regarding airway responsiveness was drawn largely from controlled human exposure studies. The evidence for respiratory illness was drawn from epidemiologic studies that reported associations between respiratory symptoms and indoor exposures to NO_2 in people living in homes with gas stoves. The biological plausibility of the epidemiologic results was supported by

toxicological studies that detected changes in lung host defenses following NO_2 exposure. Subpopulations considered potentially more susceptible to the effects of NO_2 included individuals with preexisting respiratory disease, children, and the elderly.

1.2.3 Assessment from Previous Review

In the previous review of the NO_2 NAAQS, risks were characterized by comparing ambient monitoring data, which was used as a surrogate for exposure, with potential health benchmark levels identified from controlled human exposure studies. At the time of the review, a few studies indicated the possibility for adverse health effects due to short-term (e.g., 1-hour) exposures between 0.20 ppm and 0.30 ppm NO_2. Therefore, the focus of the assessment was on the potential for short-term (i.e., 1-hour) exposures to NO_2 levels above potential health benchmarks in this range. The assessment used monitoring data from the years 1988-1992 and screened for sites with one or more hourly exceedances of potential short-term health effect benchmarks. Predictive models were then constructed to relate the frequency of hourly concentrations above 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-h average) indicated that the existing annual standard would provide adequate health protection against short-term exposures. This conclusion was instrumental in providing the rationale for the decision in the last review to retain the existing annual standard.

1.3 SCOPE OF THE RISK AND EXPOSURE ASSESSMENT FOR THE CURRENT REVIEW

NO_x include multiple gaseous (e.g., NO_2, NO, HONO) and particulate (e.g., nitrate) species. As discussed in the integrated review plan (2007a), the current review of the NO_2 NAAQS will focus on the gaseous species of NO_x and will not consider health effects directly associated with particulate species of NO_x. Of the gaseous species, EPA has historically determined it appropriate to specify the indicator of the standard in terms of NO_2 because the majority of the information regarding health effects and exposures is for NO_2. The current ISA

(EPA, 2008a) has found this to be the case and, therefore, NO_2 will be used as the indicator for the gaseous NO_x in the risk and exposure assessments described in this document.

2. SOURCES, AMBIENT LEVELS, AND EXPOSURES

2.1 SOURCES OF NO_2

Ambient levels of NO_2 are the product of both direct NO_2 emissions and emissions of other NO_x (e.g, NO), which can then be converted to NO_2 (for a more detailed discussion see the ISA, section 2.2). Nationally, anthopogenic sources account for approximately 87% of total NO_x emissions. Mobile sources (both on-road and off-road) account for about 60% of total anthopogenic emissions of NO_x, while stationary sources (e.g., electrical utilities and industry) account for the remainder (annex table 2.6-1). Highway vehicles represent the major mobile source component. In the United States, approximately half the mobile source emissions are contributed by diesel engines and half are emitted by gasoline-fueled vehicles and other sources (annex section 2.6.2 and Table 2.6-1). Apart from these anthopogenic sources, there are also natural sources of NO_x including microbial activity in soils, lightning, and wildfires (ISA, section 2.2.1 and annex section 2.6.2).

2.2 AMBIENT LEVELS OF NO_2

According to monitoring data, nationwide levels of ambient NO_2 (annual average) decreased 41% between 1980 and 2006 (ISA, Figure 2.4-15). Between 2003 and 2005, national mean concentrations of NO_2 were about 15 ppb for averaging periods ranging from a day to a year. The average daily maximum hourly NO_2 concentrations were approximately 30 ppb. These values are about twice as high as the 24-h averages. The highest maximum hourly concentrations (~200 ppb) between 2003 and 2005 are more than a factor of ten higher than the mean hourly or 24-h concentrations (ISA, Figure 2.4-13). The highest levels of NO_2 in the United States can be found in and around Los Angeles, in the Midwest, and in the Northeast.

Nitrogen dioxide is monitored mainly in large urban areas and, therefore, data from the NO_2 monitoring network is generally more representative of urban areas than rural areas. Levels in non-urban areas can be estimated with modeling. Model-based estimates indicate that NO_2 levels in many non-urban areas of the United States are less than 1 ppb. Levels in these areas can approach policy-relevant background concentrations, which are those concentrations that would occur in the United States in the absence of anthopogenic emissions in continental North

America (defined here as the United States, Canada, and Mexico). For NO_2, policy-relevant background concentrations are estimated to range from 0.1 ppb to 0.3 ppb (ISA, section 2.4.6).

Ambient levels of NO_2 exhibit both seasonal and diurnal variation. In southern cities, such as Atlanta, higher concentrations are found during winter, consistent with the lowest mixing layer heights being found during that time of the year. Lower concentrations are found during summer, consistent with higher mixing layer heights and increased rates of photochemical oxidation of NO_2. For cities in the Midwest and Northeast, such as Chicago and New York City, higher levels tend to be found from late winter to early spring with lower levels occurring from summer though the fall. In Los Angeles the highest levels tend to occur from autumn though early winter and the lowest levels from spring though early summer. Mean and peak concentrations in winter can be up to a factor of two larger than in the summer at sites in Los Angeles. In terms of daily variability, NO_2 levels typically peak during the morning rush hours. Monitor siting plays a key role in evaluating diurnal variability as monitors located further away from traffic will show cycles that are less pronounced over the course of a day than monitors located closer to traffic.

2.3 EXPOSURE TO NO_2

2.3.1 Overview

Human exposure to an airborne pollutant can be characterized by contact between a person and the pollutant at a specific concentration for a specified period of time (ISA, section 2.5.1). The integrated exposure of a person to a given pollutant is the time-weighted average of the exposures over all time intervals for all microenvironments in which the individual spends time. Microenvironments in which people are exposed to air pollutants such as NO_2 typically include residential indoor environments and other indoor locations, near-traffic outdoor environments and other outdoor locations, and in vehicles (ISA, Figure 2.5-1).

There is a large amount of variability in the time that individuals spend in different microenvironments, but on average people spend the majority of their time (about 87%) indoors. Most of this time is spent at home with less time spent in an office/workplace or other indoor locations (ISA, Figure 2.5-1). On average, people spend about 8% of their time outdoors and 6% of their time in vehicles. Significant variability surrounds each of these broad estimates, particularly when considering influential personal attributes such as age or gender; when

accounting for daily, weekly, or seasonal factors influencing personal behavior; or when characterizing individual variability in time spent in various locations (McCurdy and Graham, 2003; Graham and McCurdy, 2004). Typically, the time spent outdoors or in vehicles could vary by 100% or more depending on which of these influential factors are considered. One potential consequence of this is that exposure misclassification can result when total human exposure is not disaggregated between relevant microenvironments and the variability in time spent in these locations is not taken into consideration. Such misclassification, which can occur in epidemiologic studies that rely on ambient pollutant levels as a surrogate for exposure to ambient NO_2, may obscure the true relationship between ambient air pollutant exposures and health outcomes. Sections 2.3.2 and 2.3.3 (below) discuss in more detail sources of NO_2 exposure misclassification that are relevant for the current review of the NO_2 NAAQS.

2.3.2 Uncertainty Associated with the Ambient NO_2 Monitoring Method

The current approach to monitoring ambient NO_2 can introduce uncertainty into exposure estimates. For example, the method for estimating ambient NO_2 levels (i.e., subtraction of NO from a measure of total NO_x) is subject to interference by NO_x oxidation products. Limited evidence suggests that these compounds result in an overestimate of NO_2 levels by roughly 20 to 25% at typical ambient levels. Smaller relative errors are estimated to occur in measurements taken near strong NO_x sources since most of the mass emitted as NO or NO_2 would not yet have been further oxidized. Relatively larger errors appear in locations more distant from strong local NO_x sources. Additionally, many NO_2 monitors are elevated above ground level in the cores of large cities. Because most sources of NO_2 are near ground level, this produces a gradient of NO_2 with higher levels near ground level and lower levels being detected at the elevated monitor. One comparison has found an average of a 2.5-fold increase in NO_2 concentration measured at 4 meters above the ground compared to 15 meters above the ground. Levels are likely even higher at elevations below 4 meters (ISA, section 2.5.3.3). Another source of uncertainty in exposure estimates can result from monitor location. NO_2 monitors are sited for compliance with air quality standards rather than for capturing small-scale variability in NO_2 concentrations near sources such as roadway traffic. Significant gradients in NO_2 concentrations near roadways have been observed in several studies, and NO_2 concentrations have been found to be correlated with distance from roadway and traffic volume (ISA, section 2.5.3.2).

2.3.3 Uncertainty Associated with Ambient Levels as a Surrogate for Exposure

Many epidemiologic studies rely on measures of ambient NO_2 concentrations as surrogates for personal exposure to ambient NO_2. Results have been mixed regarding the appropriateness of using ambient levels of NO_2 as a surrogate for personal exposures to ambient NO_2. Studies examining the association between ambient NO_2 and personal exposure to NO_2 have generated mixed results due to 1) the prevalence of indoor sources of NO_2; 2) the spatial heterogeneity of NO_2 in study areas; 3) the seasonal and geographic variability in the infiltration of ambient NO_2; 4) differences in the time spent in different microenvironments; and 5) differences in study design. As a result, some researchers have concluded that ambient NO_2 may be a reasonable proxy for personal exposure, while others have noted that caution must be exercised (ISA, section 2.5.9). However, this source of exposure error is not expected to change the principal conclusions from NO_2 epidemiologic studies (see chapter 4 of this document) since it generally tends to reduce, rather than increase, effect estimates (ISA, section 5.2.2).

3. AT RISK POPULATIONS

3.1 OVERVIEW

Specific subpopulations are at increased risk for suffering NO_2-related health effects. This could occur because they are affected by lower levels of NO_2 than the general population (susceptibility), because they experience a larger health impact than the general population to a given level of exposure (susceptibility), and/or because they are exposed to higher levels of NO_2 than the general population (vulnerability). The term susceptibility generally encompasses innate (e.g., genetic or developmental) and/or acquired (e.g., age or disease) factors that make individuals more likely to experience effects with exposure to pollutants. Given the likely heterogeneity of individual responses to air pollution, the severity of health effects experienced by a susceptible subgroup may be much greater than that experienced by the population at large. Factors that may influence susceptibility to the effects of air pollution include age (e.g., infants, children, elderly); gender; race/ethnicity; genetic factors; and pre-existing disease/condition (e.g., obesity, diabetes, respiratory disease (e.g., asthma, chonic obstructive pulmonary disease (COPD)), cardiovascular disease, airway hyperresponsiveness, respiratory infection, adverse birth outcome) (ISA, sections 4.3.1, 4.3.5, and 5.3.2.8). In addition, some population groups are vulnerable to pollution-related effects because their air pollution exposures are higher than those of the general population. Factors that may influence vulnerability to the effects of air pollution include socioeconomic status, education level, air conditioning use, proximity to roadways, geographic location, level of physical activity, and work environment (e.g., indoor versus outdoor) (ISA, section 4.3.5). The ISA discusses factors that can confer susceptibility and/or vulnerability to air pollution with most of the discussion devoted to factors for which NO_2-specific evidence exists (ISA, section 4.3). These factors are discussed in more detail below.

3.2 SUSCEPTIBILITY: PRE-EXISTING DISEASE

A number of health conditions are believed to put individuals at greater risk for adverse events following exposure to air pollution. In general, these include asthma, COPD, respiratory infection, conduction disorders, congestive heart failure (CHF), diabetes, past myocardial infarction (MI), obesity, coronary artery disease, low birth weight/prematurity, and hypertension

(ISA, sections 4.3.1, 4.3.5, and 5.3.2.9). In addition to these conditions, epidemiologic evidence indicates that individuals with bronchial or airway hyperresponsiveness, as determined by methacholine provocation, may be at increased risk for experiencing respiratory symptoms (ISA, section 4.3.1). In considering NO_2 specifically, the ISA evaluates studies on asthmatics, individuals with cardiopulmonary disease, and diabetics (ISA, sections 4.3.1.1 and 4.3.1.2). These groups are discussed in more detail below.

Epidemiologic and controlled human exposure studies, supported by animal toxicology studies, have provided evidence for associations between NO_2 exposure and respiratory effects in asthmatics (ISA, section 4.3.1.1). The ISA found evidence from epidemiologic studies for an association between ambient NO_2 and children's hospital admissions, emergency department (ED) visits, and calls to doctors for asthma. NO_2 levels were associated with aggravation of asthma effects that include symptoms, medication use, and lung function. Time-series studies also demonstrated a relationship in children between hospital admissions or ED visits for asthma and ambient NO_2 levels, even after adjusting for co-pollutants such as particulate matter (PM) and carbon monoxide (CO) (ISA, section 4.3.1.1). Important evidence was also available from epidemiologic studies of indoor NO_2 exposures. Recent studies have shown associations with asthma attacks and severity of virus-induced asthma (ISA, section 4.3.1.1). In addition, in controlled human exposure studies, airway hyperresponsiveness in asthmatics appeared to be the most sensitive indicator of response to NO_2 (ISA, section 4.3.1.1).

Compared to asthma, less evidence is available to support cardiovascular disease as a mediator of susceptibility to NO_2. However, recent epidemiologic studies report that individuals with preexisting conditions (e.g., including diabetes, CHF, prior MI) may be at increased risk for adverse cardiac health events associated with ambient NO_2 concentrations (ISA, section 4.3.1.2). There is only limited supporting evidence from clinical or toxicological studies on potential susceptibility to NO_2 in persons with cardiovascular disease (ISA, section 4.3.1.2).

3.3 SUSCEPTIBILITY: AGE

The ISA identifies both children (i.e., <18 years of age) and older adults (i.e., >65 years of age) as groups that are potentially more susceptible than the general population to the health effects associated with ambient NO_2 concentrations (ISA, section 4.3.2). The ISA found evidence that associations of NO_2 with respiratory ED visits and hospitalizations were stronger

among children and older adults, though not all studies agreed on this issue (ISA, section 4.3.2). In addition, long-term exposure studies suggest effects in children that include impaired lung function growth, increased respiratory symptoms and infections, and onset of asthma (ISA, section 3.4 and 4.3.2). In some studies, associations between NO_2 and hospitalizations or ED visits for CVD have been observed in elderly populations. Among studies that observed positive associations between NO_2 and mortality, a comparison indicated that, in general, the elderly population was more susceptible than the non-elderly population to NO_2 effects (ISA, section 4.3.2).

3.4 SUSCEPTIBILITY: GENETICS

As noted in the ISA (section 4.3.4), genetic factors related to health outcomes and ambient pollutant exposures merit consideration. Several criteria must be satisfied in selecting and establishing useful links between polymorphisms in candidate genes and adverse respiratory effects. First, the product of the candidate gene must be significantly involved in the pathogenesis of the adverse effect of interest. Second, polymorphisms in the gene must produce a functional change in either the protein product or in the level of expression of the protein. Third, in epidemiologic studies, the issue of confounding by other environmental exposures must be carefully considered (ISA, section 4.3.4).

Investigation of genetic susceptibility to NO_2 effects has focused on the glutathione S-tranferase (GST) gene. Several GST genes have common, functionally-important alleles that affect host defense in the lung (ISA, section 4.3.4). GST genes are inducible by electrophilic species (e.g., reactive oxygen species) and individuals with genotypes that result in enzymes with reduced or absent peroxide activity are likely to have reduced defenses against oxidative insult. This could potentially result in increased susceptibility to inhaled oxidants and radicals. However, data on genetic susceptibility to NO_2 are only beginning to emerge and, while it remains plausible that there are genetic factors that can influence health responses to NO_2, the few available studies do not provide specific support for genetic susceptibility to NO_2 exposure (ISA, section 4.3.4).

3.5 SUSCEPTIBILITY: GENDER

As reported in the ISA, a limited number of NO_2 studies have stratified results by gender. The results of these studies were mixed, and the ISA does not draw conclusions regarding the potential for gender to confer susceptibility to the effects of NO_2 (ISA, section 4.3.3).

3.6 VULNERABILITY: PROXIMITY (ON OR NEAR) TO ROADWAYS

The ISA includes discussion of vulnerable populations that experience increased NO_2 exposures on or near roadways (ISA, section 4.3.6). Large gradients in NOx concentrations near roadways lead to increased exposures for individuals residing, working, or attending school in the vicinity. Many studies find that indoor, personal, and outdoor NO_2 levels are strongly associated with proximity to traffic or to traffic density (ISA, section 4.3.6). Due to high air exchange rates, NO_2 levels inside a vehicle could rapidly approach levels outside the vehicle during commuting (ISA, section 4.3.6). Mean in-vehicle NO_2 levels are between 2 and 3 times ambient levels measured at fixed sites nearby (ISA, section 4.3.6). Therefore, individuals with occupations that require them to be in traffic or close to traffic (e.g., bus and taxi drivers, highway patrol officers, toll collectors) and individuals with long commutes could be exposed to relatively high levels of NO_2 compared to ambient levels. Due to the high peak exposures while driving, total personal exposure could be underestimated if exposures while commuting are not considered.

3.7 VULNERABILITY: SOCIOECONOMIC STATUS

The ISA discusses evidence that socioeconomic status (SES) modifies the effects of air pollution (section 4.3.6). Many recent studies examined modification by SES indicators on the association between mortality and PM or other indices such as traffic density, distance to roadway, or a general air pollution index (ISA, section 4.3.6). SES modification of NO_2 associations has been examined in fewer studies. For example, in a study conducted in Seoul, South Korea, community-level SES indicators modified the association of air pollution with ED visits for asthma. Of the five criteria air pollutants evaluated, NO_2 showed the strongest association in lower SES districts compared to high SES districts (Kim et al., 2007). In addition, Clougherty et al. (2007) evaluated exposure to violence (a chonic stressor) as a modifier of the effect of traffic-related air pollutants, including NO_2, on childhood asthma. The authors reported

an elevated risk of asthma with a 4.3-ppb increase in NO_2 exposure solely among children with above-median exposure to violence in their neighborhoods. Although these recent studies have evaluated the impact of SES on vulnerability to NO_2, they are too few in number to draw definitive conclusions (ISA, section 5.3.2.8).

3.8 NUMBER OF SUSCEPTIBLE/VULNERABLE INDIVIDUALS

The population potentially affected by NO_2 is large. A considerable fraction of the population resides, works, or attends school near major roadways, and these individuals are likely to have increased exposure to NO_2 (ISA, section 4.4). Based on data from the American Housing Survey, approximately 36 million individuals live within 300 feet (~90 meters) of a four-lane highway, railroad, or airport (ISA, section 4.4). Furthermore, in California, 2.3% of schools with a total enrollment of more than 150,000 students were located within ~500 feet of high-traffic roads, with a higher proportion of non-white and economically disadvantaged students attending those schools (ISA, section 4.4). Of this population, those with physiological susceptibility will have even greater risks of health effects related to NO_2. In the United States, approximately 10% of adults and 13% of children have been diagnosed with asthma, and 6% of adults have been diagnosed with COPD (ISA, section 4.4). The prevalence and severity of asthma is higher among certain ethnic or racial groups such as Puerto Ricans, American Indians, Alaskan Natives, and African Americans (ISA, section 4.4). Furthermore, a higher prevalence of asthma among persons of lower SES and an excess burden of asthma hospitalizations and mortality in minority and inner-city communities have been observed (ISA, section 4.4). In addition, population groups based on age also comprise substantial segments of the population that may be potentially at risk for NO_2-related health impacts. Based on U.S. census data from 2000, about 72.3 million (26%) of the U.S. population are under 18 years of age, 18.3 million (7.4%) are under 5 years of age, and 35 million (12%) are 65 years of age or older. Hence, large proportions of the U.S. population are in age groups that are likely to have increased susceptibility and vulnerability for health effects from ambient NO_2 exposure. The considerable size of the population groups at risk indicates that exposure to ambient NO_2 could have a significant impact on public health in the United States.

4. HEALTH EFFECTS

4.1 INTRODUCTION

The ISA, along with its associated annexes, provides a comprehensive review and assessment of the scientific evidence related to the health effects associated with NO_2 exposures. For these health effects, the ISA characterizes judgments about causality with a hierarchy (for discussion see ISA, section 1.3) that contains the following five levels.

- Sufficient to infer a causal relationship
- Sufficient to infer a likely causal relationship (i.e., more likely than not)
- Suggestive but not sufficient to infer a causal relationship
- Inadequate to infer the presence or absence of a causal relationship
- Suggestive of no causal relationship

Judgments about causality are informed by a series of criteria that are based on those set forth by Sir Austin Bradford Hill in 1965 (ISA, table 1.3-1). These criteria include strength of the observed association, availability of experimental evidence, consistency of the observed association, biological plausibility, coherence of the evidence, temporal relationship of the observed association, and the presence of an exposure-response relationship. The judgments of the ISA, along with the rationale supporting those judgments, are presented below.

4.2 ADVERSE RESPIRATORY EFFECTS FOLLOWING SHORT-TERM EXPOSURES

4.2.1 Overview

The ISA concludes that, taken together, recent studies provide scientific evidence that is sufficient to infer a likely causal relationship between short-term NO_2 exposure and adverse effects on the respiratory system (ISA, section 5.3.2.1). This finding is supported by the large body of recent epidemiologic evidence as well as findings from human and animal experimental studies. These epidemiologic and experimental studies encompass a number of endpoints including ED visits and hospitalizations, respiratory symptoms, airway hyperresponsiveness, airway inflammation, and lung function. Effect estimates from epidemiologic studies conducted in the United States and Canada generally indicate a 2-20% increase in risks for ED visits and

hospital admissions and higher risks for respiratory symptoms (ISA, section 5.4). The findings relevant to these endpoints, which provide the rationale to support the judgment of a likely causal relationship, are described in more detail below.

4.2.2 Respiratory Emergency Department Visits and Hospitalizations

Epidemiologic evidence exists for positive associations of short-term ambient NO_2 concentrations below the current NAAQS with increased numbers of ED visits and hospital admissions for respiratory causes, especially asthma (ISA, section 5.3.2.1). Total respiratory causes for ED visits and hospitalizations typically include asthma, bronchitis and emphysema (collectively referred to as COPD), pneumonia, upper and lower respiratory infections, and other minor categories. Temporal associations between ED visits or hospital admissions for respiratory diseases and ambient levels of NO_2 have been the subject of over 50 peer-reviewed research publications since the last review of the NO_2 NAAQS. These studies have examined morbidity in different age groups and have often utilized multi-pollutant models to evaluate potential confounding effects of co-pollutants. Associations are particularly consistent among children and older adults (65+ years) when all respiratory outcomes are analyzed together (ISA, figures 3.1-8 and 3.1-9) and among children and subjects of all ages for asthma admissions (ISA, figures 3.1-12 and 3.1-13). When examined with co-pollutant models, associations of NO_2 with respiratory ED visits and hospital admissions were generally robust and independent of the effects of co-pollutants (ISA, figures 3.1-10 and 3.1-11). The plausibility and coherence of these effects are supported by experimental (i.e., toxicologic and controlled human exposure) studies that evaluate host defense and immune system changes, airway inflammation, and airway responsiveness (see subsequent sections of this document and ISA, section 5.3.2.1).

Of the ED visit and hospital admission studies reviewed in the ISA, 6 key studies were conducted in the United States (ISA, table 5.4-1). Of these 6 studies, 4 evaluated associations with NO_2 using multi-pollutant models (Peel et al., 2005 and Tolbert et al., 2007 in Atlanta; New York Department of Health (NYDOH), 2006 and Ito et al., 2007 in New York City) while 2 studies used only single pollutant models (Linn et al., 2000; Jaffe et al., 2003). In the study by Peel and colleagues, investigators evaluated ED visits among all ages in Atlanta, GA during the period of 1993 to 2000. Using single pollutant models, the authors reported a 2.4% (95% CI: 0.9, 4.1) increase in respiratory ED visits associated with a 30-ppb increase in 1-h max NO_2

concentrations. For asthma visits, a 4.1% (95% CI: 0.8%, 7.6%) increase was detected in individuals 2 to 18 years of age. Tolbert and colleagues reanalyzed these data with 4 additional years of information and found essentially similar results in single pollutant models (2.0% increase, 95% CI: 0.5, 3.3). This same study found that the associations were positive, but not statistically-significant, in multi-pollutant models that included PM_{10} or ozone (O_3). In the study conducted by the New York Department of Health, investigators evaluated asthma ED visits in Bronx and Manhattan, New York over the period of January, 1999 to November, 2000. In Bronx, the authors found a 6% (95% CI: 1%-10%) increase in visits per 20 ppb increase in 24-h average concentrations of NO_2 and a 7% increase in visits per 30 ppb increase in daily 1-h maximum concentrations. These effects were not statistically-significant in 2-pollutant models that included $PM_{2.5}$ or SO_2. In Manhattan, the authors found non-significant decreases (3% for 24-h and a 2% for daily 1-h maximum) in ED visits associated with increasing NO_2. In the study by Ito and colleagues, investigators evaluated ED visits for asthma in New York City during the years 1999 to 2002. The authors found a 12 % (95% CI: 7%, 15%) increase in risk per 20 ppb increase in 24-h ambient NO_2. Risk estimates were robust and remained statistically significant in multi-pollutant models that included $PM_{2.5}$, O_3, CO, and SO_2.

4.2.3 Respiratory Symptoms

Evidence for associations between NO_2 and respiratory symptoms is derived primarily from the epidemiologic literature, although the experimental evidence for airway inflammation and immune system effects (described in the ISA, section 3.1 and summarized in subsequent sections of this document) does provide some plausibility and coherence for the epidemiologic results (ISA, section 5.3.2.1). Consistent evidence has been observed for an association of respiratory effects with indoor and personal NO_2 exposures in children (ISA, sections 3.1.5.1 and 5.3.2.1) and with ambient levels of NO_2 as measured by community monitors (ISA, sections 3.1.4.2 and 5.3.2.1, see Figure 3.1-6). In the results of multi-pollutant models, NO_2 associations in multicity studies are generally robust to adjustment for co-pollutants including O_3, CO, and PM_{10} (ISA, section 5.3.2.1 and Figure 3.1-7). Specific studies of respiratory symptoms are discussed in more detail below.

Studies of Ambient NO_2

Epidemiologic studies using community ambient monitors have found associations between ambient NO_2 concentrations and respiratory symptoms (ISA, sections 3.1.4.2 and 5.3.2.1, Figure 3.1-6) in cities where NO_2 concentrations were within the range of 24-h average concentrations observed in recent years. Several studies have been published since the last review of the NO_2 NAAQS including single-city studies (e.g., Ostro et al., 2001; Delfino et al., 2002) and multi-city studies in urban areas covering the continental United States and southern Ontario (Schwartz et al., 1994; Mortimer et al., 2002; Schildcrout et al., 2006). The multi-city studies are discussed in more detail below.

Schwartz el at (1994) studied 1,844 schoolchildren, followed for 1 year, as part of the Six Cities Study that included the cities of Watertown, MA, Baltimore, MD, Kingston-Harriman, TN, Steubenville, OH, Topeka, KS, and Portage, WI. Respiratory symptoms were recorded daily. The authors reported a significant association between 4-day mean NO_2 levels and incidence of cough among all children in single-pollutant models, with an odds ratio (OR) of 1.61 (95% CI: 1.08, 2.43) standardized to a 20-ppb increase in NO_2. The incidence of cough increased up to approximately mean NO_2 levels (~13 ppb) ($p = 0.01$), after which no further increase was observed. The significant association between cough and 4-day mean NO_2 level remained unchanged in models that included O_3 but lost statistical significance in two-pollutant models that included PM_{10} (OR = 1.37 [95% CI: 0.88, 2.13]) or SO_2 (OR = 1.42 [95% CI: 0.90, 2.28]).

Mortimer et al. (2002) studied the risk of asthma symptoms among 864 asthmatic children in New York City, NY, Baltimore, MD, Washington, DC, Cleveland, OH, Detroit, MI, St Louis, MO, and Chicago, IL. Subjects were followed daily for four 2-week periods over the course of nine months with morning and evening asthma symptoms and peak flow recorded. The greatest effect was observed for morning symptoms using a 6-day moving average, with a reported OR of 1.48 (95% CI: 1.02, 2.16) per 20 ppb increase in NO_2. Although the magnitudes of effect estimates were generally robust in multi-pollutant models that included O_3 (OR for 20-ppb increase in NO_2 = 1.40 [95% CI: 0.93, 2.09]), O_3 and SO_2 (OR for NO_2 = 1.31 [95% CI: 0.87, 2.09]), or O_3, SO_2, and PM_{10} (OR for NO_2 = 1.45 [95% CI: 0.63, 3.34]), they were not statistically-significant.

Schildcrout et al. (2006) investigated the association between ambient NO_2 and respiratory symptoms and rescue inhaler use as part of the CAMP study. The study reported on 990 asthmatic children living within 50 miles of an NO_2 monitor in Boston, MA, Baltimore, MD, Toronto, ON, St. Louis, MO, Denver, CO, Albuquerque, NM, or San Diego, CA. Symptoms and use of rescue medication were recorded daily, resulting in each subject having an approximate average of two months of data. The authors reported the strongest association between NO_2 and increased risk of cough for a 2-day lag, with an OR of 1.09 (95% CI: 1.03, 1.15) for each 20-ppb increase in NO_2 occurring 2 days before measurement. Multi-pollutant models that included CO, PM_{10}, or SO_2 produced similar results (ISA, Figure 3.1-5, panel A). Additionally, increased NO_2 exposure was associated with increased use of rescue medication, with the strongest association for a 2-day lag, both for single- and multi-pollutant models (e.g., for an increase of 20-ppb NO_2 in the single-pollutant model, the RR for increased inhaler usage was 1.05 (95% CI: 1.01, 1.09).

Studies of Indoor NO_2

Evidence supporting increased respiratory morbidity following NO_2 exposures is also found in studies of indoor NO_2 (ISA, section 3.1.4.1). For example, in a randomized intervention study in Australia (Pilotto et al., 2004), students attending schools that switched out unvented gas heaters, a major source of indoor NO_2, experienced a decrease in both levels of NO_2 and in respiratory symptoms (e.g., difficulty breathing, chest tightness, and asthma attacks) compared to students in schools that did not switch out unvented gas heaters (ISA, section 3.1.4.1). An earlier indoor study by Pilotto and colleagues (1997) also found that students in classrooms with higher levels of NO_2 had higher rates of respiratory symptoms (e.g., sore thoat, cold) and absenteeism than students in classrooms with lower levels of NO_2. This study detected a significant concentration-response relationship, strengthening the argument that NO_2 is causally related to respiratory morbidity. A number of other indoor studies conducted in homes have also detected significant associations between indoor NO_2 and respiratory symptoms (ISA, section 3.1.4.1).

4.2.4 Lung Host Defenses and Immunity

Impaired host-defense systems and increased risk of susceptibility to both viral and bacterial infections after NO_2 exposures have been observed in epidemiologic, controlled human exposure, and animal toxicological studies (ISA, section 3.1.1 and 5.3.2.1). A recent

epidemiologic study (Chauhan et al., 2003) provides evidence that increased personal exposure to NO_2 worsened virus-associated symptoms and decreased lung function in children with asthma. The limited evidence from controlled human exposure studies indicates that NO_2 may increase susceptibility to injury by subsequent viral challenge at exposures of as low as 0.6 ppm for 3 hours in healthy adults (Frampton et al., 2002). Toxicological studies have shown that lung host defenses, including mucociliary clearance and immune cell function, are sensitive to NO_2 exposure, with effects observed at concentrations of less than 1 ppm (ISA, section 3.1.7). When taken together, epidemiologic and experimental studies linking NO_2 exposure with viral illnesses provide coherent and consistent evidence that NO_2 exposure can result in lung host defense or immune system effects (ISA, sections 3.1.7 and 5.3.2.1). This group of outcomes also provides some plausibility for other respiratory system effects. For example, effects on ciliary action (clearance) or immune cell function (i.e. macrophage phagocytosis) could lead to the type of outcomes assessed in epidemiologic studies, including respiratory illness or respiratory symptoms (ISA, section 5.3.2.1).

4.2.5 Airway Hyperresponsiveness

In acute exacerbations of asthma, bronchial smooth muscle contraction occurs quickly to narrow the airway in response to exposure to various stimuli including allergens or irritants. Bronchoconstriction is the dominant physiological event leading to clinical symptoms and interference with airflow (National Heart, Lung, and Blood Institute, 2007). Inhaled pollutants such as NO_2 may enhance the inherent responsiveness of the airway to a challenge by allergens or nonspecific agents (ISA, section 3.1.3). In the laboratory, airway responses can be measured by assessing changes in pulmonary function (e.g., decline in FEV_1) or changes in the inflammatory response (e.g., using markers in bronchoalveolar lavage (BAL) fluid or induced sputum) (ISA, section 3.1.3).

The ISA (section 5.3.2.1) draws two broad conclusions regarding airway responsiveness following NO_2 exposure. First, the ISA concludes that NO_2 exposure may enhance the sensitivity to allergen-induced decrements in lung function and increase the allergen-induced airway inflammatory response at exposures as low as 0.26 ppm NO_2 for 30 minutes (ISA, section 5.3.2.1 and Figure 3.1-2). Second, exposure to NO_2 has been found to enhance the inherent responsiveness of the airway to subsequent nonspecific challenges in controlled human exposure

studies (section 3.1.4.2). In general, small but significant increases in nonspecific airway responsiveness were observed in the range of 0.2 to 0.3 ppm NO_2 for 30-minute exposures and at 0.1 ppm NO_2 for 60-minute exposures in asthmatics. This enhanced airway responsiveness could have important clinical implications for asthmatics since transient increases in airway responsiveness following NO_2 exposure have the potential to increase symptoms and worsen asthma control (ISA, section 5.4). In addition, the ISA sites the controlled human exposure literature on airway hyperresponsiveness as being supportive of the epidemiologic evidence on respiratory morbidity (ISA, section 5.4). Because studies on airway hyperresponsiveness have been used to identify potential health effect benchmark values and to inform the identification of potential alternative standards for evaluation (see sections 4.5 and 5 of this document), more detail is provided below on the specific studies that form the basis for the conclusions in the ISA regarding this endpoint.

Folinsbee (1992) conducted a meta-analysis using individual level data from 19 clinical NO_2 exposure studies measuring airway responsiveness in asthmatics (ISA, section 3.1.3.2). These studies included NO_2 exposure levels between 0.1 ppm and 1.0 ppm and most of them used nonspecific bronchoconstricting agents such as methacholine, carbachol, histamine, or cold air. The largest effects were observed for subjects at rest. Among subjects exposed at rest, 76% experienced increased airway responsiveness following exposure to NO_2 levels between 0.2 and 0.3 ppm. Results from an update of this meta-analysis (results combined only from nonspecific responsiveness studies) are presented in the ISA (Table 3.1-3) and in Table 4-1 below.

Table 4-1. Fraction of nitrogen dioxide-exposed asthmatics with increased nonspecific airway hyperresponsiveness[2]

NO_2 ppm	ALL EXPOSURES	EXPOSURE WITH EXERCISE	EXPOSURE AT REST
0.1	0.66 (50)[B]	—	0.66 (50)[B]
0.1 - 0.15	0.68 (87)[C]	0.59 (17)	0.67 (70)[C]
0.2 - 0.3	0.58 (187)[B]	0.52 (136)	0.75 (51)[C]
> 0.3	0.59 (81)	0.49 (48)	0.73 (33)[B]
0.1 - 0.6	0.60 (355)[C]	0.52 (201)	0.71 (154)[C]

[2] Values are the fraction of asthmatics (out of the total number of individuals in parenthesis) having an increase in airway responsiveness following NO_2 versus air exposure. See table 3.1-3 in the ISA for more detail. [B] indicates $p \leq 0.05$ and [C] indicates $p \leq 0.01$.

As noted in Table 4-1, when exposed at rest 66% of subjects experienced an increase in airway responsiveness following exposure to 0.1 ppm NO_2, 67% of subjects experienced an increase in airway responsiveness following exposure to NO_2 concentrations between 0.1 and 0.15 ppm (inclusively), 75% of subjects experienced an increase in airway responsiveness following exposure to NO_2 concentrations between 0.2 and 0.3 ppm (inclusively), and 73% of subjects experienced an increase in airway responsiveness following exposure to NO_2 concentrations above 0.3 ppm. Effects of NO_2 exposure on the direction of airway responsiveness are statistically-significant at all of these levels. Because this meta-analysis evaluates only the direction of the change in airway responsiveness, it is not possible to discern the magnitude of the change from these data. However, the results do suggest that short-term exposures to NO_2 at near-ambient levels (<0.3 ppm) can alter airway responsiveness in people with mild asthma (ISA, section 3.1.3.2).

Several studies published since the last review address the question of whether low-level exposures to NO_2 enhance the response to specific allergen challenge in mild asthmatics (ISA, section 3.1.3.1). These recent studies suggest that NO_2 may enhance the sensitivity to allergen-induced decrements in lung function and increase the allergen-induced airway inflammatory response. Strand et al. (1997) demonstrated that single 30-minute exposures to 0.26-ppm NO_2 increased the late phase response to allergen challenge 4 hours after exposure, as measured by changes in lung function. In a separate study (Strand et al., 1998), 4 daily repeated exposures to 0.26-ppm NO_2 for 30 minutes increased both the early and late-phase responses to allergen, as measured by changes in lung function. Barck et al. (2002) used the same exposure and challenge protocol in the earlier Strand study (0.26 ppm for 30 min, with allergen challenge 4 hours after exposure), and performed BAL 19 hours after the allergen challenge to determine NO_2 effects on the allergen-induced inflammatory response. Compared with air followed by allergen, NO_2 followed by allergen caused an increase in the BAL recovery of polymorphonuclear (PMN) cells and eosinophil cationic protein (ECP) as well as a reduction in total BAL fluid volume and cell viability. ECP is released by degranulating eosinophils, is toxic to respiratory epithelial cells, and is thought to play a role in the pathogenesis of airway injury in asthma. Subsequently, Barck et al. (2005) exposed 18 mild asthmatics to air or 0.26 ppm NO_2 for 15 minutes on day 1, followed by two 15 minute exposures separated by 1 hour on day 2, with allergen challenge after exposures on both days 1 and 2. Sputum was induced before exposure on day 1 and after

exposures (morning of day 3). Compared to air plus allergen, NO_2 plus allergen resulted in increased levels of ECP in both sputum and blood and increased myeloperoxidase levels in blood. All exposures in these studies (Barck et al., 2002, 2005; Strand et al., 1997, 1998) used subjects at rest. They used an adequate number of subjects, included air control exposures, randomized exposure order, and separated exposures by at least 2 weeks. Together, they indicate the possibility for effects on allergen responsiveness in some asthmatics following brief exposures to 0.26 ppm NO_2. However, other recent studies have failed to find effects using similar, but not identical, approaches (ISA, section 3.1.3.1). The differing findings may relate in part to differences in timing of the allergen challenge, the use of multiple versus single-dose allergen challenge, the use of BAL versus sputum induction, exercise versus rest during exposure, and differences in subject susceptibility (ISA, section 3.1.3.1).

4.2.6 Airway Inflammation

Effects of NO_2 on airway inflammation have been observed in controlled human exposure and animal toxicological studies at higher than ambient levels (0.4-5 ppm). The few available epidemiologic studies were suggestive of an association between ambient NO_2 concentrations and inflammatory response in the airway in children, though the associations were inconsistent in the adult populations examined (ISA, section 3.1.2 and 5.3.2.1). Controlled human exposure studies provide evidence for increased airway inflammation at NO_2 concentrations of <2.0 ppm. The onset of inflammatory responses in healthy subjects appears to be between 100 and 200 ppm-minutes, i.e., 1 ppm for 2 to 3 hours (ISA, Figure 3.1-1). Increases in biological markers of inflammation were not observed consistently in healthy animals at levels of less than 5 ppm; however, increased susceptibility to NO_2 concentrations of as low as 0.4 ppm was observed when lung vitamin C was reduced (by diet) to levels that were <50% of normal. These data provide some evidence for biological plausibility and one potential mechanism for other respiratory effects, such as exacerbation of asthma symptoms and increased ED visits for asthma (ISA, section 5.3.2.1).

4.2.7 Lung Function

Recent epidemiologic studies that examined the association between ambient NO_2 concentrations and lung function in children and adults generally produced inconsistent results (ISA, sections 3.1.5.1 and 5.3.2.1). Controlled human exposure studies generally did not find

direct effects of NO_2 on lung function in healthy adults at levels as high as 4.0 ppm (ISA, section 5.3.2.1). For asthmatics, the direct effects of NO_2 on lung function also have been inconsistent at exposure concentrations of less than 1 ppm NO_2.

4.2.8 Conclusions and Coherence of Evidence for Short-Term Respiratory Effects

As noted previously, the ISA concludes that the findings of epidemiologic, controlled human exposure, and animal toxicological studies provide evidence that is sufficient to infer a likely causal relationship for respiratory effects following short-term NO_2 exposure (ISA, sections 3.1.7 and 5.3.2.1). The ISA (section 5.4) concludes that the strongest evidence for an association between NO_2 exposure and adverse human health effects comes from epidemiologic studies of respiratory symptoms, ED visits, and hospital admissions. These studies include panel and field studies, studies that control for the effects of co-occurring pollutants, and studies conducted in areas where the whole distribution of ambient 24-h average NO_2 concentrations was below the current NAAQS level of 0.053 ppm (53 ppb) (annual average). The effect estimates from the U.S. and Canadian studies generally indicate a 2-20% increase in risks for ED visits and hospital admissions. Risks associated with respiratory symptoms are generally higher (ISA, section 5.4).

Overall, the epidemiologic evidence for respiratory effects can be characterized as consistent, in that associations are reported in studies conducted in numerous locations with a variety of methodological approaches. Considering this large body of epidemiologic studies alone, the findings are also coherent in the sense that the studies report associations with respiratory health outcomes that are logically linked together. In addition, a number of these associations are statistically-significant, particularly the more precise effect estimates (ISA, section 5.3.2.1). These epidemiologic studies are supported by evidence from toxicological and controlled human exposure studies, particularly by controlled human exposure studies that evaluate airway hyperresponsiveness in asthmatic individuals (ISA, section 5.4). Together, the epidemiologic and experimental data sets form a plausible, consistent, and coherent description of a relationship between NO_2 exposures and an array of adverse health effects that range from the onset of respiratory symptoms to hospital admission.

However, as noted in the ISA (section 5.4), it is difficult to determine "the extent to which NO_2 is independently associated with respiratory effects or if NO_2 is a marker for the

effects of another traffic-related pollutant or mix of pollutants." On-road vehicle exhaust emissions are a nearly ubiquitous source of combustion pollutant mixtures that include NO_x and can be an important contributor to NO_2 levels in near-road locations. Although this complicates the efforts to quantify specific NO_2-related health effects, the evidence summarized in the ISA indicates that NO_2 associations generally remain robust in multi-pollutant models and supports a direct effect of short-term NO_2 exposure on respiratory morbidity at ambient concentrations below the current NAAQS level. The robustness of epidemiologic findings to adjustment for co-pollutants, coupled with data from animal and human experimental studies, support the determination that the relationship between NO_2 and respiratory morbidity is likely causal, while still recognizing the relationship between NO_2 and other traffic related pollutants.

4.3 OTHER ADVERSE EFFECTS FOLLOWING SHORT-TERM EXPOSURES

The ISA concludes that the epidemiologic evidence is suggestive but not sufficient to infer a causal relationship between short-term exposure to NO_2 and all-cause and cardiopulmonary-related mortality (ISA, section 5.3.2.3). Results from several large U.S. and European multi-city studies and a meta-analysis study indicate positive associations between ambient NO_2 concentrations and the risk of all-cause (nonaccidental) mortality, with effect estimates ranging from 0.5 to 3.6% excess risk in mortality per standardized increment (20 ppb for 24-h averaging time, 30 ppb for 1-h averaging time) (ISA, section 3.3.1, Figure 3.3-2, section 5.3.2.3). In general, the NO_2 effect estimates were robust to adjustment for co-pollutants. Both cardiovascular and respiratory mortality have been associated with increased NO_2 concentrations in epidemiologic studies (ISA, Figure 3.3-3); however, similar associations were observed for other pollutants, including PM and SO_2. The range of risk estimates for excess mortality is generally smaller than that for other pollutants such as PM. In addition, while NO_2 exposure, alone or in conjunction with other pollutants, may contribute to increased mortality, evaluation of the specificity of this effect is difficult. Clinical studies showing hematologic effects and animal toxicological studies showing biochemical, lung host defense, permeability, and inflammation changes with short-term exposures to NO_2 provide limited evidence of plausible pathways by which risks of mortality may be increased, but no coherent picture is evident at this time (ISA, section 5.3.2.3).

The ISA concludes that the available evidence on cardiovascular health effects following short-term exposure to NO_2 is inadequate to infer the presence or absence of a causal relationship at this time (ISA, section 5.3.2.2). Evidence from epidemiologic studies of heart rate variability, repolarization changes, and cardiac rhythm disorders among heart patients with ischemic cardiac disease are inconsistent (ISA, section 5.3.2.2). In most studies, associations with PM were found to be similar or stronger than associations with NO_2. Generally positive associations between ambient NO_2 concentrations and hospital admissions or ED visits for cardiovascular disease have been reported in single-pollutant models (ISA, section 5.3.2.2); however, most of these effect estimate values were diminished in multi-pollutant models that also contained CO and PM indices (ISA, section 5.3.2.2). Mechanistic evidence of a role for NO_2 in the development of cardiovascular diseases from studies of biomarkers of inflammation, cell adhesion, coagulation, and thombosis is lacking (ISA, section 5.3.2.2). Furthermore, the effects of NO_2 on various hematological parameters in animals are inconsistent and, thus, provide little biological plausibility for effects of NO_2 on the cardiovascular system (ISA, section 5.3.2.2).

4.4 ADVERSE EFFECTS FOLLOWING LONG-TERM EXPOSURES

4.4.1 Respiratory Morbidity

The ISA concludes that overall, the epidemiologic and experimental evidence is suggestive but not sufficient to infer a causal relationship between long-term NO_2 exposure and respiratory morbidity (ISA, section 5.3.2.4). The available database evaluating the relationship between respiratory illness in children and long-term exposures to NO_2 has increased since the last review of the NO_2 NAAQS. A number of epidemiologic studies have examined the effects of long-term exposure to NO_2 and reported positive associations with decrements in lung function and partially irreversible decrements in lung function growth (ISA, section 3.4.1, figures 3.4-1 and 3.4-2). Specifically, results from the California-based Children's Health Study, which evaluated NO_2 exposures in children over an 8-year period, demonstrated deficits in lung function growth (Gauderman et al., 2004). This effect has also been observed in Mexico City, Mexico (Rojas-Martinez et al., 2007a,b) and in Oslo, Norway (Oftedal et al., 2008), with decrements ranging from 1 to 17.5 ml per 20- ppb increase in annual NO_2 concentration. Similar associations have been found for PM, O_3, and proximity to traffic (<500 m), though these studies did not report the results of co-pollutant models. The high correlation among traffic-related

pollutants makes it difficult to accurately estimate independent effects in these long-term exposure studies (ISA, section 5.3.2.4). With regard to asthma incidence and long-term NO_2, two major cohort studies, the Children's Health Study (Gauderman et al., 2005) and a birth cohort study in the Netherlands (Brauer et al., 2007), observed significant associations. However, several other studies failed to find consistent associations between long-term NO_2 exposure and asthma outcomes (ISA, section 5.3.2.4). Similarly, epidemiologic studies conducted in the United States and Europe have produced inconsistent results regarding an association between long-term exposure to NO_2 and respiratory symptoms (ISA, sections 3.4.3 and 5.3.2.4). While some positive associations were noted, a large number of symptom outcomes were examined and the results across specific outcomes were inconsistent (ISA, section 5.3.2.4).

Animal toxicological studies may provide biological plausibility for the chonic effects of NO_2 that have been observed in epidemiologic studies (ISA, sections 3.4.5 and 5.3.2.4). The main biochemical targets of NO_2 exposure appear to be antioxidants, membrane polyunsaturated fatty acids, and thiol groups. NO_2 effects include changes in oxidant/antioxidant homeostasis and chemical alterations of lipids and proteins. Lipid peroxidation has been observed at NO_2 exposures as low as 0.04 ppm for 9 months and at exposures of 1.2 ppm for 1 week, suggesting lower effect thesholds with longer durations of exposure. Other studies showed decreases in formation of key arachidonic acid metabolites in AMs following NO_2 exposures of 0.5 ppm. NO_2 has been shown to increase collagen synthesis rates at concentrations as low as 0.5 ppm. This could indicate increased total lung collagen, which is associated with pulmonary fibrosis, or increased collagen turnover, which is associated with remodeling of lung connective tissue. Morphological effects following chonic NO_2 exposures have been identified in animal studies that link to these increases in collagen synthesis and may provide plausibility for the deficits in lung function growth described in epidemiologic studies (ISA, section 3.4.5).

4.4.2 Mortality

The ISA concludes that the epidemiologic evidence is inadequate to infer the presence or absence of a causal relationship between long-term exposure to NO_2 and mortality (ISA, section 5.3.2.6). In the United States and European cohort studies examining the relationship between long-term exposure to NO_2 and mortality, results have been inconsistent (ISA, section 5.3.2.6).

Further, when associations were suggested, they were not specific to NO_2 but also implicated PM and other traffic indicators. The relatively high correlations reported between NO_2 and PM indices make it difficult to interpret these observed associations at this time (ISA, section 5.3.2.6).

4.4.3 Other Long-Term Effects

The ISA concludes that the available epidemiologic and toxicological evidence is inadequate to infer the presence or absence of a causal relationship for carcinogenic, cardiovascular, and reproductive and developmental effects related to long-term NO_2 exposure (ISA, section 5.3.2.5). Epidemiologic studies conducted in Europe have shown an association between long-term NO_2 exposure and increased incidence of cancer (ISA, section 5.3.2.5). However, the animal toxicological studies have provided no clear evidence that NO_2 acts as a carcinogen (ISA, section 5.3.2.5). The very limited epidemiologic and toxicological evidence does not suggest that long-term exposure to NO_2 has cardiovascular effects (ISA, section 5.3.2.5). The epidemiologic evidence is not consistent for associations between NO_2 exposure and growth retardation; however, some evidence is accumulating for effects on preterm delivery (ISA, section 5.3.2.5). Scant animal evidence supports a weak association between NO_2 exposure and adverse birth outcomes and provides little mechanistic information or biological plausibility for the epidemiologic findings.

4.5 RELEVANCE OF SPECIFIC HEALTH EFFECTS TO THE NO_2 RISK CHARACTERIZATION

4.5.1 Overview

As described previously, the ISA characterizes judgments about causality with a hierarchy (for discussion see ISA, section 1.3) that contains the following five levels.

- Sufficient to infer a causal relationship
- Sufficient to infer a likely causal relationship (i.e., more likely than not)
- Suggestive but not sufficient to infer a causal relationship
- Inadequate to infer the presence or absence of a causal relationship
- Suggestive of no causal relationship

For purposes of the quantitative characterization of NO_2 health risks, staff has judged it appropriate to focus on endpoints for which the ISA concludes that the available evidence is sufficient to infer either a causal or a likely causal relationship. The only endpoint meeting either of these criteria is respiratory morbidity following short-term NO_2 exposure. The ISA (section 5.4) concludes that the "epidemiologic, controlled human exposure and animal toxicologic studies provided evidence that short-term NO_2 exposures can result in adverse impacts to public health at current ambient concentrations (mean 24-h avg concentrations ranging from 3–70 ppb [Table 5.4-1]). In particular, a set of coherent and consistent respiratory health outcomes were associated with short-term NO_2 exposures including exacerbated asthma and other respiratory symptoms, increased airway hyperresponsiveness, inflammation, impaired host defense, aggravated viral infections, and increased ED visits and hospital admissions." Therefore, for purposes of characterizing health risks associated with NO_2, we have focused on respiratory morbidity endpoints that have been associated with short-term NO_2 exposures. Other endpoints (e.g., long-term effects) will be considered as part of the evidence-based evaluation of potential alternative standards during the rulemaking stage of the NAAQS review. In evaluating the appropriateness of specific endpoints for use in the NO_2 risk characterization, we have considered both epidemiologic and controlled human exposure studies.

4.5.2 Epidemiology

The ISA characterizes the epidemiologic evidence for respiratory effects as consistent, in that associations are reported in studies conducted in numerous locations and with a variety of methodological approaches (ISA, section 5.3.2.1). The findings are also coherent in the sense that the studies report associations with respiratory health outcomes that are logically linked together (ISA, section 5.3.2.1). When the epidemiologic literature is considered as a whole, there are generally positive associations between NO_2 and respiratory symptoms, hospitalization, and ED visits. A number of these associations are statistically significant, particularly the more precise effect estimates (ISA, section 5.3.2.1). However, the ISA (section 5.4) offers the following caveat to consider when interpreting the epidemiologic results: "It is difficult to determine from these new studies the extent to which NO_2 is independently associated with respiratory effects or if NO_2 is a marker for the effects of another traffic-related pollutant or mix of pollutants (see Section 5.2.2 for more details on exposure issues). A factor contributing to

uncertainty in estimating the NO_2-related effect from epidemiologic studies is that NO_2 is a component of a complex air pollution mixture from traffic related sources that include CO and various forms of PM." These caveats should be considered when interpreting a quantitative NO_2 risk estimate based on the epidemiology literature. Despite these uncertainties, the ISA (section 5.4) concludes that, "Although this complicates the efforts to disentangle specific NO_2-related health effects, the evidence summarized in this assessment indicates that NO_2 associations generally remain robust in multi-pollutant models and supports a direct effect of short-term NO_2 exposure on respiratory morbidity at ambient concentrations below the current NAAQS. The robustness of epidemiologic findings to adjustment for copollutants, coupled with data from animal and human experimental studies, support a determination that the relationship between NO_2 and respiratory morbidity is likely causal, while still recognizing the relationship between NO_2 and other traffic related pollutants." Therefore, epidemiologic studies have been judged to be an appropriate basis for a quantitative assessment of the risks associated with ambient NO_2.

When selecting specific epidemiologic studies on which to base the risk assessment, staff has considered several factors. First, we have judged that studies conducted in the United States are preferable to those conducted outside the United States given the potential for effect estimates to be impacted by factors such as the ambient pollutant mix, the placement of monitors, activity patterns of the population, and characteristics of the healthcare system. Second, we judged that studies of ambient NO_2 are preferable to those of indoor NO_2 given that studies of indoor NO_2 focus on exposures in locations with indoor sources of NO_2. These indoor sources can result in exposure patterns, NO_2 levels, and co-pollutants that are different from those typically associated with ambient NO_2. Third, we judged it appropriate to focus on studies of ED visits and hospital admissions. When compared to studies of respiratory symptoms, the public health significance of ED visits and hospital admissions are less ambiguous (e.g., because of the potential disconnect between health outcomes and subjective symptom ratings). In addition, baseline incidence data are more readily available for these endpoints. Finally, we judged it appropriate to focus on studies that evaluated NO_2 health effect associations using both single- and multi-pollutant models. Taking these factors into consideration, we have chosen to focus on the studies by Peel and colleagues (2005) and by Tolbert and colleagues (2007) in Atlanta, Georgia. The epidemiology-based risk assessment is described in more detail in subsequent sections of this document.

4.5.3 Controlled Human Exposure Studies

Controlled human exposure studies have addressed the consequences of short-term (e.g., 30-minutes to several hours) NO_2 exposures for a number of health endpoints including airway responsiveness, host defense and immunity, inflammation, and lung function (ISA, section 3.1). In identifying health endpoints from controlled human exposure studies on which to focus the characterization of NO_2 health risks, staff judges it appropriate to focus on endpoints that occur at or near ambient levels of NO_2 and endpoints that are of clinical significance. With regard to the NO_2 levels at which different effects have been documented, the ISA concludes that 1) in asthmatics NO_2 may increase the allergen-induced airway inflammatory response at exposures as low as 0.26-ppm for 30 min (ISA, Figure 3.1-2) and NO_2 exposures between 0.2 and 0.3 ppm for 30 minutes or 0.1 ppm for 60-minutes can result in small but significant increases in nonspecific airway responsiveness (ISA, section 5.3.2.1); 2) limited evidence indicates that NO_2 may increase susceptibility to injury by subsequent viral challenge following exposures of 0.6-1.5 ppm for 3 hours; 3) evidence exists for increased airway inflammation at NO_2 concentrations less than 2.0 ppm; and 4) the direct effects of NO_2 on lung function in asthmatics have been inconsistent at exposure concentrations below 1 ppm (ISA, section 5.3.2.1). The ISA notes that epidemiologic studies have reported health effects associations in areas reporting maximum ambient concentrations from 100 to 300 ppb (ISA, Tables 5.3-2 and 5.3-3). Therefore, of the health effects caused by NO_2 in controlled human exposure studies, the only effect identified by the ISA to occur at or near ambient levels is airway hyperresponsiveness in asthmatics.

The airway response can vary dramatically between individuals, ranging from mild to severe and spanning orders of magnitude (ISA, section 4.3.1.1). When discussing the clinical significance of NO_2-related airway hyperresponsiveness, the ISA concludes that "transient increases in airway responsiveness following NO_2 exposure have the potential to increase symptoms and worsen asthma control" (ISA, sections 3.1.3 and 5.4). That this effect could have public health implications is suggested by the large size of the asthmatic population in the United States (see above and ISA, Table 4.4-1). In addition, NO_2 effects on airway responsiveness are part of the body of experimental evidence that provides plausibility and coherence for the effects observed on hospital admissions and ED visits in epidemiologic studies (ISA, section 5.3.2.1). Therefore, although studies on several of the endpoints evaluated in controlled human exposure studies provide qualitative support for the ability of NO_2 to cause adverse effects on respiratory

health, the focus for purpose of quantifying risks associated with ambient NO_2 is airway responsiveness (see below).

Because many of the studies of airway responsiveness evaluate only a single level of NO_2 and because of methodological differences between the studies, staff has judged that the data are not sufficient to derive an exposure-response relationship in the range of interest. Therefore, the most appropriate approach to characterizing risks based on the controlled human exposure evidence for airway responsiveness is to compare estimated NO_2 air quality and exposure levels with potential health effect benchmark levels. Estimates of hourly peak air quality concentrations and personal exposures to ambient NO_2 concentrations at and above specified potential health effect benchmark levels provide some perspective on the potential public health impacts of NO_2 exposure. Staff recognizes that there is high inter-individual variability in NO_2-induced effects on airway responsiveness such that only a subset of asthmatic individuals exposed at and above a given benchmark level may actually be expected to experience an adverse effect.

To identify potential health effect benchmarks, staff has relied on the ISA's evaluation of the NO_2 human exposures studies. Controlled human exposure studies involving allergen challenge in asthmatics suggest that NO_2 exposure may enhance the sensitivity to allergen-induced decrements in lung function and increase the allergen-induced airway inflammatory response at exposures as low as 0.26-ppm NO_2 for 30 min (ISA, Figure 3.1-2 and section 5.3.2.1). Exposure to NO_2 also has been found to enhance the inherent responsiveness of the airway to subsequent nonspecific challenges (ISA, section 5.3.2.1). In asthmatics, small but significant increases in nonspecific airway responsiveness have been observed in the range of 0.2 to 0.3 ppm NO_2 for 30 minute exposures and at 0.1 ppm NO_2 for 1-h exposures (ISA, section 5.3.2.1). Therefore, for the risk characterization, staff judges that 1-h NO_2 levels in this range are appropriate to consider as potential health benchmarks for comparison to air quality levels and exposure estimates. To characterize health risks with respect to this range, potential health effect benchmark values of 0.10 ppm, 0.20 ppm, 0.25 ppm, and 0.30 ppm have been employed to reflect the lower- middle- and upper-end of the range identified in the ISA as levels at which controlled human exposure studies have provided evidence for the occurrence of NO_2-induced airway hyperresponsiveness.

In choosing this range, we recognize that uncertainties exist regarding the percentage of asthmatics expected to experience an increase in responsiveness following NO_2 exposure and in the clinical implications of such an increase. A meta-analysis presented in the ISA (see Table 4-1 above) suggests that between 66% and 75% of asthmatics may experience an increase in airway responsiveness following short-term NO_2 exposures in the range of 0.1 to 0.3 ppm. However, this meta-analysis provides information only on the direction of the NO_2 effect and not on its magnitude. In addition, the NO_2 controlled human exposure studies of airway responsiveness have focused primarily on mild asthmatics. It is possible that more severely affected asthmatics could experience a more severe response following NO_2 exposures in this range. It is also possible that they could experience a response at lower levels of NO_2 than the mild asthmatics included in these studies. However, even considering these uncertainties, staff judges that the identified range of concentrations is sufficient to provide some perspective on the potential public health impacts of NO_2 exposures, especially when the results of the risk characterization based on airway responsiveness are considered in conjunction with the risk assessment based on the epidemiology literature.

5. IDENTIFICATION OF POTENTIAL ALTERNATIVE STANDARDS FOR ANALYSIS

5.1 INTRODUCTION

The primary goals of the NO_2 risk and exposure assessment described in this draft document are to estimate short-term exposures and potential human health risks associated with 1) recent levels of ambient NO_2; 2) NO_2 levels associated with just meeting the current standard; and 3) NO_2 levels associated with just meeting potential alternative standards. This section identifies potential alternative standards in terms of indicator, averaging time, form, and level and provides the rationale that was used to select them.

5.2 INDICATOR

The NO_x include multiple gaseous (e.g., NO_2, NO) and particulate (e.g., nitrate) species. In considering the appropriateness of different indicators, we note that the health effects associated with particulate species of NO_x have been considered within the context of the health effects of ambient particles in the Agency's review of the NAAQS for PM. Thus, as discussed in the integrated review plan (2007a), the current review of the NO_2 NAAQS is focused on the gaseous species of NO_x and will not consider health effects directly associated with particulate species of NO_x. Of the gaseous species, EPA has historically determined it appropriate to specify the indicator of the standard in terms of NO_2 because the majority of the information regarding health effects and exposures is for NO_2. The final ISA has found that this continues to be the case and, therefore, staff believes that NO_2 remains the most appropriate indicator.

5.3 AVERAGING TIME

The current annual standard for NO_2 was originally set in 1971 based on epidemiologic studies that supported a link between adverse respiratory effects and long-term exposure to low-levels of NO_2. Although the quantitative basis for the annual averaging time was later called into question (60 FR 52876), the annual standard was retained in the most recent review (60 FR 52876) for two key reasons. First, the evidence showing the most serious health effects associated with long-term exposures (e.g., emphysematous-like alterations in the lung and increased susceptibility to infection) came from animal studies conducted at concentrations well

above those permitted in the ambient air by the annual standard. Second, an air quality assessment conducted by EPA concluded that areas that meet the annual standard would be unlikely to experience short-term peaks above levels that had been shown in controlled human exposure studies to impact endpoints of potential concern (i.e., airway responsiveness).

The issue of averaging time will be reconsidered in the current review. As described above, the ISA concludes that, when taken together, "recent studies provide scientific evidence that NO_2 is associated with a range of respiratory effects and is sufficient to infer a likely causal relationship between short-term NO_2 exposure and adverse effects on the respiratory system" (ISA, section 5.3.2.1). This conclusion is based, in part, on the observation that a number of epidemiologic studies have detected positive associations between short-term (e.g., 1-h, 24-h) NO_2 concentrations and health effects. Many of these studies have been conducted in locations where long-term ambient levels of NO_2 are well below the current annual standard. As a result, staff has concluded that it is appropriate to consider alternative averaging times for their ability to protect against health effects associated with short-term NO_2 levels and/or exposures.

In contrast to the conclusion in the ISA concerning respiratory morbidity associated with short-term exposures to NO_2, the ISA concludes that the "evidence examining the effect of long-term exposure to NO_2 on respiratory morbidity is suggestive but not sufficient to infer a causal relationship" (ISA, section 5.3.2.4). In addition, the ISA concludes that the available evidence for the effect of long-term exposure to NO_2 on other health outcomes (i.e., mortality, cancer, cardiovascular effects, reproductive and developmental effects) is "inadequate to infer the presence or absence of a causal relationship" (ISA, sections 5.3.2.5 and 5.3.2.6). As a result, staff has not considered alternative long-term standards in the current assessment.

In considering appropriate short-term averaging times, staff has considered evidence from both experimental and epidemiologic studies. New evidence from controlled human exposure studies generally evaluates exposures between 30 minutes and 3 hours while epidemiologic studies have used different short-term averaging periods, most commonly 1-h and 24-h (ISA, section 3.1). A few epidemiologic studies have considered both 1-h and 24-h averaging times, allowing comparisons to be made. The ISA reports that such comparisons failed to reveal differences between effect estimates based on a 1-h averaging time versus those based on a 24-h averaging time (ISA, section 5.3.2.7). Therefore, the ISA concludes that it is not possible to discern whether effects observed in epidemiologic studies are attributable to average daily (or

multiday) concentrations (24-h avg) or high, peak exposures (1-h max) (ISA, section 5.3.2.7). In addition, the ISA concludes that experimental studies in both animals and humans provide evidence that NO_2 exposures from less than 1 hour up to 3 hours can result in respiratory effects (section 5.3.2.7). Given that the epidemiologic evidence does not provide clear guidance in choosing between 1-h and 24-h averaging times, and given that the experimental literature provides support for the occurrence of effects following exposures of shorter duration than 24 hours (e.g., 1-h), staff has chosen to evaluate standards with a 1-h averaging time.

5.4 FORM

In evaluating alternative forms for the primary standard, staff recognizes that it is important to have a form that 1) reflects the health risks posed by elevated NO_2 concentrations and 2) achieves a balance between limiting the occurrence of peak concentrations and providing a stable and robust regulatory target. Consistent with judgments made in recent reviews of the PM (71 FR 61144) and O_3 (73 FR 16436) NAAQS, staff judges that a concentration-based form for the NO_2 standard would better reflect health risks and would provide greater stability than a form based on expected exceedances. A concentration-based form gives proportionally greater weight to hours when concentrations are well above the level of the standard than to hours when the concentrations are just above the standard, while an expected exceedance form would give the same weight to an hour that just exceeds the standard as to an hour that greatly exceeds the standard. Therefore, a concentration-based form better reflects the health risks posed by elevated NO_2 concentrations and, in developing potential alternative standards for consideration, we have focused on standards with concentration-based forms. The most recent review of the PM NAAQS (completed in 2006) judged that using a 98^{th} percentile form averaged over 3 years provides an appropriate balance between limiting the occurrence of peak concentrations and providing a stable regulatory target (71 FR 61144). In that review, staff also considered other forms within the range of the 95^{th} to the 99^{th} percentiles. In making recommendations regarding the form, staff considered the impact on risk of different forms, the year-to-year stability in the air quality statistic, and the extent to which different forms of the standard would allow different numbers of days per year to be above the level of the standard in areas that achieve the standard. Based on these considerations, staff recommended either a 98^{th} percentile form or a 99^{th} percentile form. We have made similar judgments in identifying an appropriate range of forms

for potential alternative NO_2 standards. As a result of these judgments, we have determined it appropriate to consider both the 98th and 99th percentile NO_2 concentrations averaged over 3 years. We have judged that these percentiles, when combined with the range of alternatives identified for the level of the standard (see below), offer a sufficient range of options to balance the objective of providing a stable regulatory target against the objective of limiting the occurrence of peak concentrations.

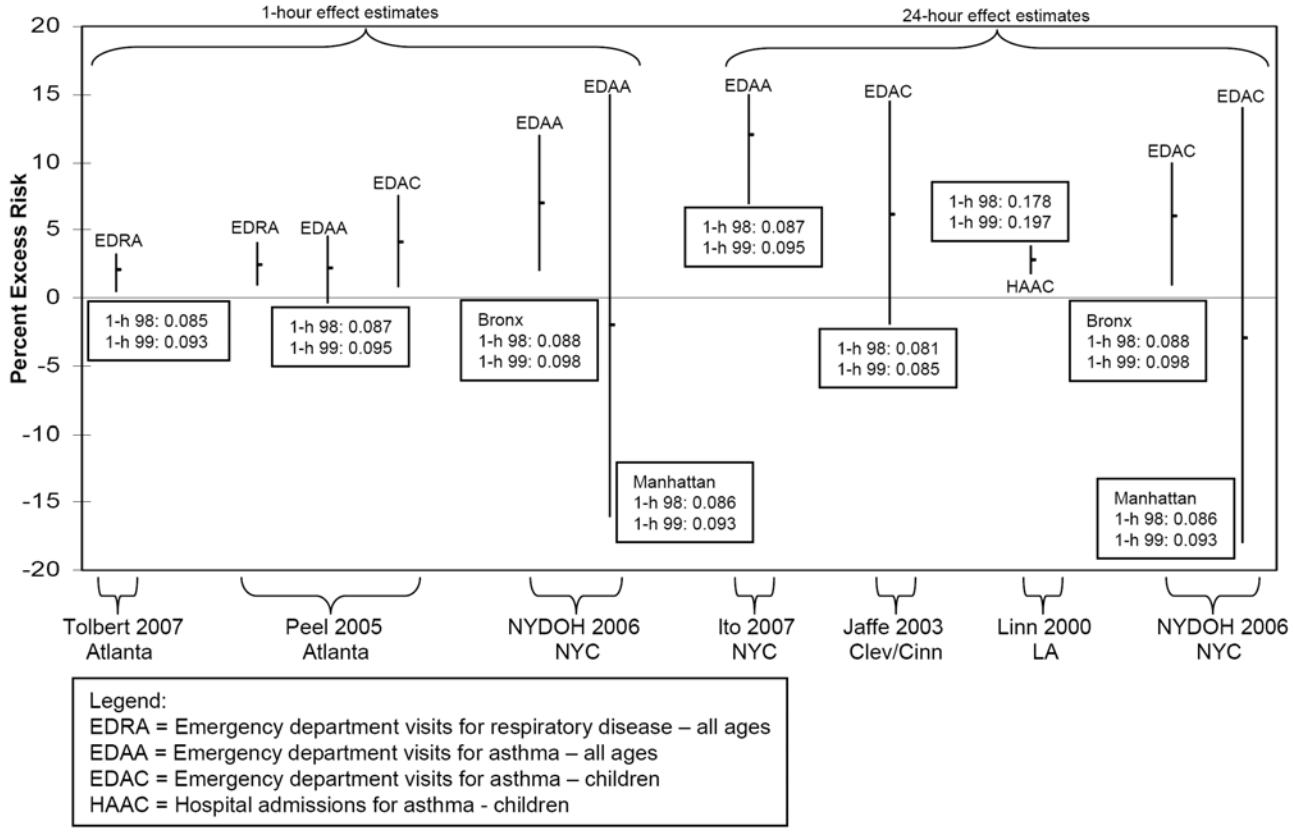
5.5 LEVEL

In developing an approach to formulating an appropriate range of NO_2 levels for analysis, staff has taken into account several considerations including the following. First, since the last review of the NO_2 NAAQS, a large number of published epidemiologic studies have evaluated associations between respiratory morbidity and short-term levels of ambient NO_2. In general, these studies report positive associations and a number of these associations are statistically-significant. The ISA notes that many of these studies have been conducted in locations where ambient levels of NO_2 are well below the level of the current NAAQS (ISA, section 5.3.2.1). Second, controlled human exposure studies have detected effects of NO_2 exposure on several health endpoints. Of these, only airway hyperresponsiveness is associated with exposures to NO_2 concentrations at or near ambient levels. In fact, the NO_2 exposure levels associated with increased airway responsiveness overlap the maximum ambient NO_2 concentrations in some locations where associations with respiratory effects have been detected. Third, limitations in both epidemiologic studies (e.g., confounding by co-pollutants) and controlled human exposure studies (e.g., most sensitive populations likely not evaluated) suggest that an appropriate approach to identifying levels for potential alternative standards is to consider both types of studies. Therefore, to determine the levels that should be evaluated, staff has relied on both key epidemiologic studies conducted in the United States that evaluate associations between short-term levels of NO_2 and respiratory morbidity (symptoms, hospital admissions, ED visits) and on controlled human exposure studies that evaluate airway hyperresponsiveness following NO_2 exposure. Figures 5-1 and 5-2 below show standardized effect estimates[3] and the 98th and 99th percentile concentrations of daily 1-h maximum NO_2 for locations and time periods that

[3] The effect estimates presented in figures 5-1 and 5-2 are for those endpoints included in figure 5.3-1 and table 5.4-1 of the ISA.

correspond to key U.S. epidemiologic studies identified in the ISA (see table 5.4-1 in ISA for a list of key studies).

Of the key U.S. epidemiologic studies included in figures 5-1 and 5-2, the highest 1-h NO_2 concentrations were detected in the two studies conducted in Los Angeles (Linn et al., 2000; Ostro et al., 2001). For these studies, the 98^{th} and 99^{th} percentile 1-h daily maximum concentrations of NO_2 overlap levels that the ISA concludes are associated with increased airway responsiveness in controlled human exposure studies (ISA, section 5.3.2.1). Therefore, staff judges that the combination of the epidemiologic studies by Linn et al. (2000) and Ostro et al. (2001), as well as the meta-analysis (Folinsbee, 1992; ISA, table 3.1-3; table 4-1 of this document) of controlled human exposure studies on airway responsiveness, provide an appropriate basis for identifying the upper end of the range of standard levels to be considered. Given that the ISA concludes that significant increases in airway responsiveness are associated with short-term exposures to NO_2 at 0.2 to 0.3 ppm and given that the epidemiologic studies by Linn et al. (2000) and Ostro et al. (2001) are associated with 98^{th} and 99^{th} percentile 1-h daily maximum NO_2 levels that are just below (Linn et al., 2000) and just above (Ostro et al., 2001) 0.2 ppm (see figures 1 and 2 below), staff judges that an appropriate upper end of the range of potential standard levels is a daily maximum 1-h NO_2 concentration of 0.20 ppm.



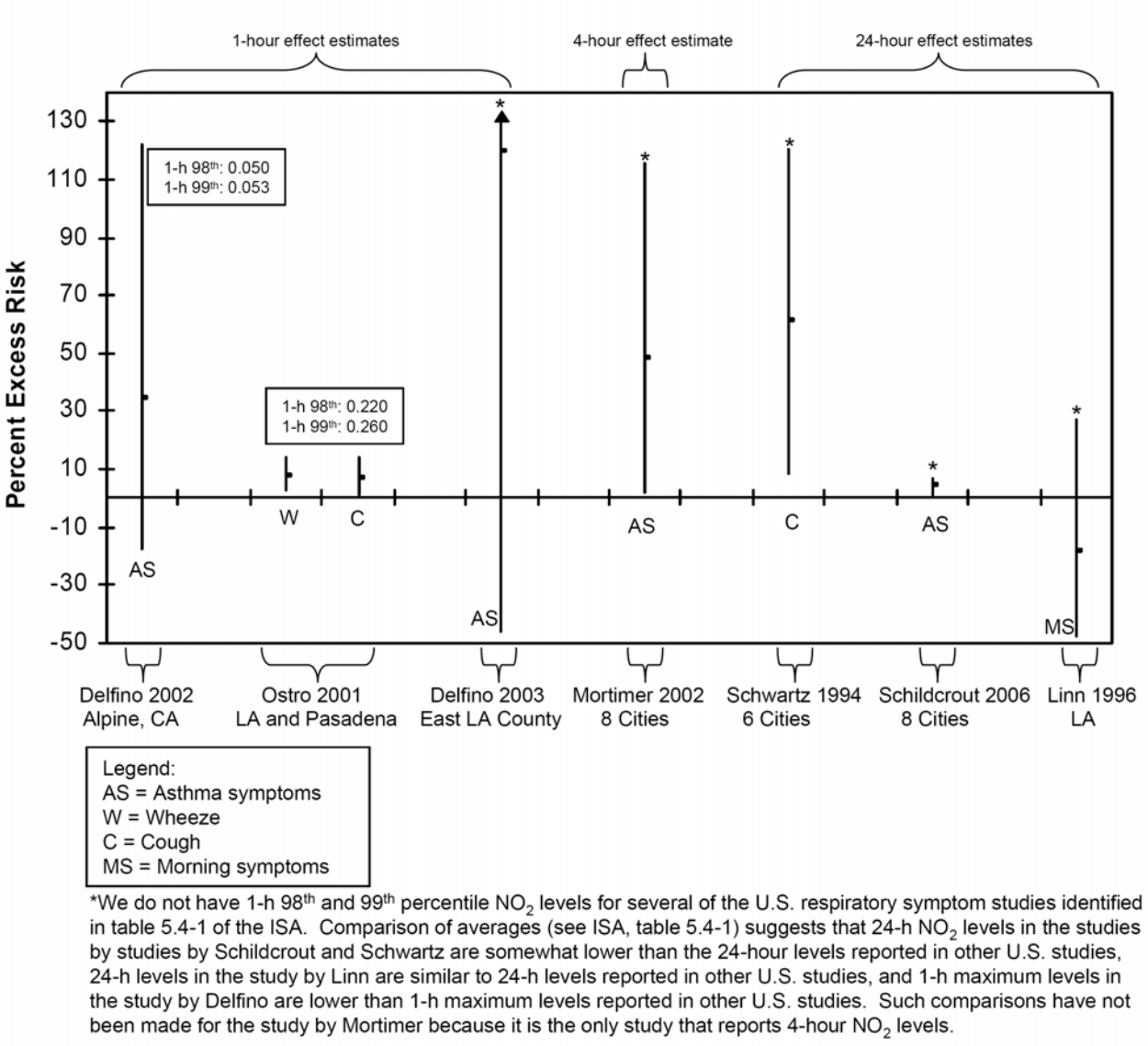
1

Figure 5-1. NO_2 effect estimates[4] (95% CI) for ED visits/HA and associated 1-h daily maximum NO_2 levels (98^{th} and 99^{th} percentile values in boxes[5])

2

[4]Effect estimates presented in figures 5-1 and 5-2 are from single pollutant models only. The studies by Tolbert et al., (2007); Peel et al., (2005); NYDOH (2006); Ito et al., (2007); and Delfino et al. (2002) also evaluated multi-pollutant models. NO_2 effect estimates retained statistical-significance in the study by Ito, but not in the other studies.

[5] Authors of relevant U.S. and Canadian studies were contacted and air quality statistics from the study monitor that recorded the highest NO_2 levels were requested. In cases where authors provided 1-hour daily maximum air quality statistics, this information is presented in figures 1 and 2 (studies by Tolbert, Peel, NYDOH, Delfino). In one case (study by Ito) authors provided 24-hour air quality data, but identified a specific monitor in AQS. We used AQS to reconstruct the 1-hour daily maximum air quality for that monitor during the time period of the study. In three cases (studies by Jaffe, Linn, Ostro), we were not able to identify appropriate statistics from the information provided by the authors and the authors did not provide monitor identification information. In these cases, we attempted to reconstruct the air quality data set for the location and time of the study using EPA's Air Quality System (AQS). We have not yet received air quality information from any of the Canadian authors contacted and we were unable to reconstruct the air quality data sets for the Canadian studies. Therefore, for purposes of identifying levels of potential alternative standards, our analysis was based on these key U.S. studies.



*We do not have 1-h 98th and 99th percentile NO_2 levels for several of the U.S. respiratory symptom studies identified in table 5.4-1 of the ISA. Comparison of averages (see ISA, table 5.4-1) suggests that 24-h NO_2 levels in the studies by studies by Schildcrout and Schwartz are somewhat lower than the 24-hour levels reported in other U.S. studies, 24-h levels in the study by Linn are similar to 24-h levels reported in other U.S. studies, and 1-h maximum levels in the study by Delfino are lower than 1-h maximum levels reported in other U.S. studies. Such comparisons have not been made for the study by Mortimer because it is the only study that reports 4-hour NO_2 levels.

Figure 5-2. NO_2 effect estimates for respiratory symptoms and associated 1-h daily maximum NO_2 levels (98th and 99th percentile values in boxes)

In identifying additional standard levels that should be analyzed, staff has considered that 1) health effect associations in epidemiologic studies are observed in locations with 1-h daily maximum levels of NO_2 below 0.2 ppm (i.e., 99th percentile levels in several studies are close to 0.1 ppm); 2) controlled human exposure studies that evaluate the ability of NO_2 to elicit airway hyperresponsiveness have assessed mild asthmatics and more severely affected asthmatics could experience increased airway responsiveness at lower levels of NO_2 than observed in these studies; and 3) a meta-analysis presented in the ISA (see Table 4-1) detects statistically-

significant effects on the direction of airway responsiveness following short-term NO_2 exposures as low as 0.1 ppm. As a result of these considerations, staff judges that it would be appropriate to consider additional standard levels that provide a margin of safety relative to 0.20 ppm. Therefore, we will also consider daily maximum 1-h NO_2 standard levels of 0.10 ppm and 0.15 ppm.

In identifying the lower end of the range of standards that will be analyzed, staff has considered the fact that the study by Delfino et al., (2002) provides evidence for associations between short-term ambient NO_2 concentrations and respiratory morbidity in a location where the 98^{th} and 99^{th} percentile concentrations of the 1-h daily maximum levels of NO_2 were well below 0.1 ppm (Delfino et al., 2002). This study detects associations between 1-h and 8-h (only 8-h associations were statistically-significant) levels of NO_2 and asthma symptoms in a location where the 98^{th} and 99^{th} percentile 1-h daily maximum NO_2 concentrations were 0.050 and 0.053 ppm, respectively. The 8-h effect estimate in this study remained positive, but became statistically non-significant, in a two-pollutant model that also included PM_{10}. Staff judges that it is appropriate to base the lower end of the range of alternative standard levels on this study by Delfino et al. (2002). Therefore, we will also consider a 1-h daily maximum standard level of 0.050 ppm.

6. OVERVIEW OF APPROACHES TO ASSESSING EXPOSURES AND RISKS

6.1 INTRODUCTION

The purpose of the assessments described in this document is to characterize exposures and risks associated with recent ambient levels of NO_2, with levels associated with just meeting the current NO_2 NAAQS, and with levels associated with just meeting potential alternative standards (see chapter 5 of this document for discussion of potential alternative standards). To characterize health risks, we have employed thee approaches. With each approach, we have characterized health risks associated with the air quality scenarios of interest (i.e., recent air quality unadjusted, air quality adjusted to simulate just meeting the current standard, and air quality adjusted to simulate just meeting potential alternative standards). In the first approach, NO_2 air quality levels have been compared to potential health effect benchmark values derived from the controlled human exposure literature. In the second approach, modeled estimates of actual exposures have been compared to potential health effect benchmarks. In the third approach, exposure-response relationships from epidemiologic studies have been used to estimate health impacts. An overview of the approaches to characterizing health risks is provided below and each approach is described in more detail in subsequent sections of this document and the associated appendices.

In the first approach, we have compared NO_2 air quality with potential health effect benchmark levels for NO_2. Scenario-driven air quality analyses have been performed using ambient NO_2 concentrations for the years 1995 though 2006. With this approach, NO_2 air quality serves as a surrogate for exposure. All U.S. monitoring sites where NO_2 data have been collected are represented by this analysis and, as such, the results generated are considered a broad characterization of national air quality and human exposures that might be associated with these concentrations. An advantage of this approach is its relative simplicity; however, there is uncertainty associated with the assumption that NO_2 air quality can serve as an adequate surrogate for exposure to ambient NO_2. Actual exposures might be influenced by factors not considered by this approach, such as the spatial and temporal variability in human activities.

In the second approach, we have used an inhalation exposure model to generate more realistic estimates of personal exposures. Estimates of personal exposure have been compared to potential NO_2 health benchmark levels. For this exposure analysis, a probabilistic approach was used to model individual exposures considering the time people spend in different microenvironments and the variable NO_2 concentrations that occur within these microenvironments across time, space, and microenvironment type. This approach to assessing exposures was more resource intensive than using ambient levels as a surrogate for exposure; therefore, staff has included the analysis of only one specific location in the U.S. (Atlanta MSA)[6]. Although the geographic scope of this analysis is restricted, the approach provides realistic estimates of NO_2 exposures, particularly those exposures associated with important emission sources of NO_x and NO_2, and serves to complement to the broad air quality characterization.

For the characterization of risks in both the air quality analysis and the exposure modeling analysis described above, staff has used a range of short-term potential health effect benchmarks. The levels of potential benchmarks are based on NO_2 exposure levels that have been associated with increased airway responsiveness in asthmatics in controlled human exposure studies (ISA, section 5.3.2.1; see above for discussion). Benchmark values of 100, 150, 200, 250, and 300 ppb have been compared to both NO_2 air quality levels and to estimates of NO_2 exposure. When NO_2 air quality is used as a surrogate for exposure, the output of the analysis is an estimate of the number of times per year specific locations experience 1-h levels of NO_2 that exceed a particular benchmark. When personal exposures are simulated, the output of the analysis is an estimate of the number of individuals at risk for experiencing daily maximum 1-h levels of NO_2 of ambient origin that exceed a particular benchmark. An advantage of using potential health effect benchmark levels to characterize health risks is that the effects observed in controlled human exposure studies clearly result from NO_2 exposure. This is in contrast to health effects associated with NO_2 in epidemiologic studies, which may also be associated with pollutants that co-occur with NO_2 in the ambient air. Thus, when using epidemiologic studies as the basis for risk characterization, the unique contribution of NO_2 to a particular health effect

[6] In the document titled *Risk and Exposure Assessment to Support the Review of the NO_2 Primary National Ambient Air Quality Standard: First Draft*, we have presented the results of an exposure analysis for Philadelphia. Based on CASAC comments received on that exposure analysis, we have refined our approach and applied those refinements to the Atlanta analysis presented in this document. The original Philadelphia analysis is presented in the appendix to this document, but has not been modified since the first draft.

may be difficult to quantify. A disadvantage of the potential benchmark approach is that the magnitude of the NO_2 effect on airway responsiveness can vary considerably from individual to individual and not all asthmatics would be expected to respond to the same levels of NO_2 exposure. Therefore, the public health impacts of NO_2-induced airway hyperresponsiveness are difficult to quantify.

In the third approach, we have estimated respiratory ED visits as a function of ambient levels of NO_2 measured at a fixed-site monitor representing ambient air quality for an urban area. In this approach, concentration-response functions are derived from NO_2 epidemiologic studies and are used to estimate the impact of ambient levels of NO_2, as measured at a fixed-site monitor, on ED visits. By focusing on a different health endpoint from the first two approaches described above, this epidemiology-based approach provides additional perspective on the potential public health impacts of NO_2. Relative to the approaches that use controlled human exposure studies, this approach to characterizing health risks has several advantages. For example, the public health significance of the effect in question (i.e., ED visits) is less ambiguous in terms of its impact on an individual than in the case of airway hyperresponsiveness. In addition, the concentration-response relationship reflects real-world levels of NO_2 and co-pollutants present in ambient air. However, a disadvantage of this approach is the ambiguity and complexity associated with quantifying the contribution of NO_2 to the reported health impacts relative to the contributions of co-occurring pollutants.

6.2 SIMULATING THE CURRENT AND ALTERNATIVE STANDARDS

A primary goal of this draft of the risk and exposure assessments is to evaluate the ability of the current NO_2 standard (0.053 ppm annual average) and potential alternative standards (see chapter 5 of this document) to protect public health. In order to evaluate the ability of a specific standard to protect public health, NO_2 concentrations need to be adjusted such that they simulate levels of NO_2 that just meet that standard. For example, all areas of the United States currently have ambient NO_2 levels below the current annual standard. Therefore, to simulate just meeting the current annual standard, NO_2 air quality levels must be rolled upward. Similarly, to simulate a potential standard that is below current air quality levels, those current levels must be rolled downward. This process of adjusting air quality to simulate just meeting a specific standard is described in more detail below. For purposes of illustration, the adjustment to simulate just

meeting the current standard is described. However, adjustments to simulate just meeting the potential alternative standards have been accomplished using the same proportional approach.

6.2.1 Adjustment of Ambient Air Quality

Based on the form of the current standard and observed trends in ambient monitoring, ambient NO_2 concentrations were proportionally rolled-up at each location using the maximum annual average concentration that occurred in each year. While annual average concentrations have declined significantly over the time period of analysis, the variability in the concentrations, both the annual average and 1-hour concentrations, have remained relatively constant (see section 7 in Appendix A for details). Therefore, proportional adjustment factors F for each location (i) and year (j) were derived by the following:

$$F_{ij} = 53 / C_{\max,ij} \qquad \text{equation (6-1)}$$

where,

F_{ij} = Adjustment factor (unitless)
$C_{max,ij}$ = Maximum annual average NO_2 concentration at a monitor in a location i and year j (ppb)

In these cases where staff simulated a proportional roll-up in ambient NO_2 concentrations using equation (6-1), it is assumed that the current temporal and spatial distribution of air concentrations (as characterized by the current air quality data) is maintained and increased NO_x emissions contribute to increased NO_2 concentrations, with the highest monitor (in terms of annual averages) being adjusted so that it just meets the current 0.053 ppm annual average standard. Values for each air quality adjustment factor used for each location evaluated in the air quality and risk characterization are given in Appendix A (section 7.2). For each location and calendar year, all the hourly concentrations in a location were multiplied by the same constant value F to make the highest annual mean equal to 53 ppb for that location and year. For example, of several monitors measuring NO_2 in Boston for year 1995, the maximum annual mean concentration was 30.5 ppb, giving an adjustment factor of $F = 53/30.5 = 1.74$ for that year. All hourly concentrations measured at all monitoring sites in that location would then be multiplied by 1.74, resulting in an upward scaling of hourly NO_2 concentrations for that year. Therefore, one monitoring site in Boston for year 1995 would have an annual average

concentration of 0.053 ppm, while all other monitoring sites would have an annual average concentration below that value, although still proportionally scaled up by 1.74. Then, using the adjusted hourly concentrations to simulate just meeting the current standard, the metrics of interest (e.g., annual mean NO_2 concentration, the number of potential health effect benchmark exceedances) were estimated for each site-year.

Proportional adjustment factors were also derived considering the form, averaging time, and levels of the potential alternative standards under consideration. Discussion regarding the staff selection of each of these components is provided in chapter 5 of this document. The 98th and 99th percentile 1-hour NO_2 concentrations averaged across three years of monitoring were used in calculating the adjustment factors at each of four levels as follows:

$$F_{ij} = S / C_{\%ile,ij} \qquad \text{equation (6-2)}$$

where,

F_{ij} = Adjustment factor (unitless)
S = Alternative standard level (50, 100, 150, 200 ppb 1-hour concentration)
$C_{\%ile,ij}$ = Maximum 98th or 99th percentile 1-hour NO_2 concentration averaged across three years at a monitor in location i (ppb)

As described above for adjustments made in simulating just meeting the current standard, it is assumed that the current temporal and spatial distribution of air concentrations (as characterized by the current air quality data) is maintained and increased NO_x emissions contribute to increased NO_2 concentrations, with the highest monitor (in terms of the 3-year average at the 98th or 99th percentile) being adjusted so that it just meets the level of the particular 1-hour alternative standard. Since the alternative standard levels range from 50 ppb through 200 ppb, both proportional roll-up and roll-backs were used to adjust the 1-hour concentrations. The values for each air quality adjustment factor used for each location evaluated in the air quality and risk characterization are given in Appendix A, section 7.2. Only the more recent air quality data were used and separated into two 3-year periods, 2001-2003 and 2004-2006. The 1-hour concentrations were adjusted in a similar manner described above for just meeting the current standard, however, due to the form of the standard, only one factor was derived for each 3-year period, rather than one factor for each calendar year as was done with just meeting the current standard.

6.2.2 Adjustment of Potential Health Effect Benchmark Levels

Rather than proportionally modify the air quality concentrations used for input to the exposure model, a proportional roll-down of the potential health effect benchmark level was performed. This was done to reduce the processing time associated with the exposure modeling simulations since there were tens of thousands of receptors modeled in each location. In addition, because the adjustment is proportional, the application of a roll-down of the selected benchmark level is mathematically equivalent to a proportional roll-up of the air quality concentrations. The same approach used in the air quality adjustment described above was used in the exposure modeling to scale the benchmark levels downward to simulate just meeting the current standard. For example, an adjustment factor of 2.27 was determined for Atlanta for year 2001 to simulate ambient concentrations just meeting the current standard, based on a maximum predicted annual average NO_2 concentration of 23.3 ppb for a modeled receptor placed at an ambient monitoring location. Therefore, the 1-hour potential health effect benchmark levels of 100, 200, and 300 ppb were proportionally rolled-down to 44, 88, and 132 ppb, respectively for year 2001. This procedure was applied for each year within each location where an exposure modeling was performed to simulate just meeting the current standard. Additional details regarding derivation of the adjusted benchmark levels are given in chapter 8 of this document.

7. AMBIENT AIR QUALITY ASSESSMENT AND HEALTH RISK CHARACTERIZATION

7.1 OVERVIEW

Ambient monitoring data for each of the years 1995 through 2006 were used in this analysis to characterize NO_2 air quality across the U.S. This air quality data, as well as other NO_2 concentrations derived from ambient levels, were used as a surrogate to estimate potential human exposure. While an individual ambient monitor measures NO_2 concentrations at a stationary location, the monitor may well represent the concentrations that persons residing nearby are exposed to. The extrapolation of ambient monitor concentration to personal exposure will be dependent upon the spatial distribution of important emission sources, the siting of the ambient monitors, and consideration of places that persons visit. It is within this context that the approach for evaluating the ambient NO_2 air quality was designed.

Based on the health effects information from the human clinical and epidemiological studies, the averaging time of interest for the air quality characterization was 1-hour, with concentration levels ranging from between 100 and 300 ppb. Since the current standard is based on annual average levels of NO_2 while the most definitive health effects evidence is associated with short-term (i.e., 30-minute to 1-hour, or one to several day) exposures, the air quality analysis required the development of a model that relates annual average and short-term levels of NO_2. To characterize this relationship and to estimate the number of exceedances of the potential health effect benchmarks in specific locations, several possible models were explored (i.e., exponential regression, logistic regression, a regression assuming a Poisson distribution, and an empirical model). An empirical model, employing the annual average and hourly concentrations, was chosen to avoid some of the difficulties in extrapolating outside the range of the data. In addition, an empirical model could be used for any averaging time of interest. A detailed discussion justifying the selection of this approach is provided in Appendix A, section 6.

The available NO_2 air quality were first divided into two year-groups; one contained data from years 1995-2000, representing an *historical* data set; the other contained the monitoring

years 2001-2006, representing *recent* ambient monitoring. Each of these monitoring year-groups were evaluated considering the NO_2 concentrations as they were reported and representing the conditions at that time (termed in this assessment "*as is*"). This served as the first air quality scenario, with the results within each year-group separated by monitor distance from a major road (either <100 m or ≥100 m). The ambient monitor data were categorized in this manner to account for the potential influence of vehicle emissions on concentrations measured at the monitors within close proximity to roadways. There is potential for different concentration levels measured at each of these locations (i.e., near-road versus away from road) and thus potentially different exposure concentrations experienced by those persons spending time in these locations. A second scenario used the *as is* ambient monitoring data obtained from monitors sited ≥100 m from a major road and a simplified on-road simulation approach to estimate on-road NO_2 concentrations for each of the year-groups. This scenario was developed by recognizing that vehicles are important emission sources of NO_x and NO_2 and that people spend time inside vehicles on roads.

Two additional scenarios followed in similar fashion to the *as is* air quality analysis, however these scenarios considered the ambient NO_2 concentrations simulated to just meeting the current standard of 0.053 ppm annual average and each of the alternative 1-hour standards of 50, 100, 150, and 200 ppb.[7] Due to the form of the alternative standards considered here (98^{th} and 99^{th} percentiles average over 3 years), the recent ambient monitoring data set was divided into two three-year periods, 2001-2003 and 2004-2006. Thus, the air quality characterization results are separated into two broad analyses, one using air quality as is and the other where air quality was adjusted to just meeting the current and alternative standards. Within both of these analyses, an additional simulation was performed to estimate NO_2 concentrations on roads. The first scenario described above is the only scenario that uses purely measurement data. Each of the other scenarios either uses a simulation procedure to estimate on-road concentrations (scenario 2), concentrations that just meet a particular standard level (scenario 3), or both (scenario4).

Since all of the NO_2 ambient monitoring sites are represented by this analysis, the results are considered a broad characterization of national air quality and potential human exposures that

[7] Originally, the historic data was evaluated using concentrations *as is* and for just meeting the current standard. The potential alternative standards were not evaluated using the 1995-2000 air quality. Results for evaluating air quality just meeting the current annual average standard using the historic data set are provided in Appendix A section 9.

might be associated with these scenario-driven concentrations. The output of this air quality characterization was used to estimate the number of times per year specific locations experience levels of NO_2 that may cause adverse health effects in susceptible individuals. Each location that was evaluated contained one to several monitors operating for a few to several years, generating a number of site-years of data. The number of site-years in a location were used to generate a distribution of two exposure and risk characterization metrics; the annual average concentrations and the numbers of exceedances that did (observed data) or could occur (simulated data) in a year for that location. The mean and median values were reported to represent the central tendency of each metric for the four scenarios in each air quality year-group, while the minimum value served to represent the lower bound. Since there were either multiple site-years or numerous simulations performed at each location using all available site-years of data, results for the upper percentiles included the 95^{th}, 98^{th} and 99^{th} percentiles of the distribution.

7.2 APPROACH

There were three broad steps to allow for the characterization of the air quality. The first step involved collecting, compiling, and screening the ambient air quality data collected since the prior review in 1995. A screening of the data followed to ensure consistency with the NO_2 NAAQS requirements. Then, criteria based on the current standard and the potential health effect benchmark levels were used to identify specific locations for analysis using descriptive statistical analysis of the screened data set. All other monitoring data not identified by the selected criteria were grouped into one of two non-specific categories. These locations (both the specific and non-specific) served as the geographic centers of the analysis, where application of the empirical model was done to estimate concentrations and exceedances of potential health effect benchmark levels. In addition to the use of the ambient concentrations (*as is*) and ambient concentrations just meeting the current and alternative standard levels, on-road concentrations were estimated in this air quality characterization to approximate the potential exposure and risk metrics associated with these concentrations.

7.2.1 Air Quality Data Screen

NO_2 air quality data and associated documentation from the years 1995 through 2006 were downloaded from EPA's Air Quality System (AQS) for this purpose (EPA, 2007c, d). A *site* was defined by the state, county, site code, and parameter occurrence code (POC), which

gives a 10-digit monitor ID code. As required by the NO_2 NAAQS, a valid year of monitoring data is needed to calculate the annual average concentration. A valid year at a monitoring site was comprised of 75% of valid days in a year, with at least 18 hourly measurements for a valid day (thus at least 274 or 275 valid days depending on presence of a leap year and a minimum of 4,932 or 4,950 hours). This served as the screening criterion for data used in the analysis.

Site-years of data are the total numbers of years the collective monitors in a location were in operation. Of a total of 5,243 site-years of data in the entire NO_2 1-hour concentration database, 1,039 site-years did not meet the above criterion and were excluded from any further analyses. In addition, since shorter term average concentrations are of interest, the remaining site-years of data were further screened for 75% completeness on hourly measures in a year (i.e., containing a minimum of 6,570 or 6,588, depending on presence of a leap year). Twenty-seven additional site-years were excluded, resulting in 4,177 complete site-years in the analytical database. Table 7-1 provides a summary of the site-years included in the analysis, relative to those excluded, by location and by two site-year groups.[8] The air quality data from AQS were separated into these two groups, one representing historic data (1995-2000) and the other representing more recent data (2001-2006) to represent temporal variability in NO_2 concentrations within each location. The selection of locations was a companion analysis to the screening, however, it is discussed in a separate section.

Table 7-1. Counts of complete site-years of NO_2 monitoring data.

	Number of Site-Years				Site-Years % Complete	
	Complete		Incomplete			
Location	1995-2000	2001-2006	1995-2000	2001-2006	1995-2000	2001-2006
Boston	58	47	16	34	78%	58%
Chicago	47	36	20	22	70%	62%
Cleveland	11	11	2	2	85%	85%
Denver	26	10	10	4	72%	71%
Detroit	12	12	4	1	75%	92%
Los Angeles	193	177	16	19	92%	90%
Miami	24	20	1	4	96%	83%
New York	93	81	12	24	89%	77%
Philadelphia	46	39	6	8	88%	83%
Washington	69	66	21	18	77%	79%
Atlanta	24	29	5	1	83%	97%
Colorado Springs	26	0	4	4	87%	0%
El Paso	14	30	11	0	56%	100%

[8] 14 of 18 named locations and the 2 grouped locations contained enough data to be considered valid for year 2006.

Location	Number of Site-Years				Site-Years % Complete	
	Complete		Incomplete			
	1995-2000	2001-2006	1995-2000	2001-2006	1995-2000	2001-2006
Jacksonville	6	4	0	2	100%	67%
Las Vegas	16	35	4	9	80%	80%
Phoenix	22	27	8	25	73%	52%
Provo	6	6	0	0	100%	100%
St. Louis	56	43	3	9	95%	83%
Other CMSA	1135	1177	249	235	82%	83%
Not MSA	200	243	112	141	64%	63%
Total	4177		1066		80%	

7.2.2 Selection of Locations for Air Quality Analysis

Criteria were established for selecting sites with high annual means and/or frequent exceedances of potential health effect benchmarks. Selected locations were those that had a maximum annual mean NO_2 level at a particular monitor greater than or equal to 25.7 ppb, which represents the 90th percentile across all locations and site-years, and/or had at least one reported 1-hour NO_2 level greater than or equal to 200 ppb, the lowest level of the potential health effect benchmarks. A *location* in this context would include a geographic area that encompasses more than a single air quality monitor (e.g., particular city, metropolitan statistical area (MSA), or consolidated metropolitan statistical area or CMSA). First, all monitors were identified as either belonging to a CMSA, a MSA, or neither. Then, locations of interest were identified through statistical analysis of the ambient NO_2 air quality data for each site within a location.

Fourteen locations met both selection criteria and an additional four met at least one of the criteria (see Table 7-2).[9] In addition to these 18 specific locations, the remaining sites were grouped into two broad location groupings. The *Other CMSA* location contains all the other sites that are in MSAs or CMSAs but are not in any of the 18 specified locations. The *Not MSA* location contains all the sites that are not in an MSA or CMSA. The final database for analysis included air quality data from a total of 205 monitors within the named locations, 331 monitors in the Other CMSA group, and 92 monitors in the Not MSA group.

[9] New Haven, CT, while meeting both criteria, did not have any recent exceedances of 200 ppb and contained one of the lowest maximum concentration-to-mean ratios, therefore was not separated out as a specific location for analysis.

Table 7-2. Locations selected for Tier I NO_2 Air Quality Characterization, associated abbreviations, and values of selection criteria.

Location				Maximum # of Exceedances of 200 ppb	Maximum Annual Mean (ppb)
Type[1]	Code	Description	Abbreviation		
CMSA*	1122	Boston-Worcester-Lawrence, MA-NH-ME-CT	Boston	1	31.1
CMSA	1602	Chicago-Gary-Kenosha, IL-IN-WI	Chicago	0	33.6
CMSA*	1692	Cleveland-Akron, OH	Cleveland	1	28.1
CMSA*	2082	Denver-Boulder-Greeley, CO	Denver	2	36.8
CMSA*	2162	Detroit-Ann Arbor-Flint, MI	Detroit	12	25.9
CMSA*	4472	Los Angeles-Riverside-Orange County, CA	Los Angeles	5	50.6
CMSA	4992	Miami-Fort Lauderdale, FL	Miami	3	16.8
CMSA*	5602	New York-Northern New Jersey-Long Island, NY-NJ-CT-PA	New York	3	42.2
CMSA*	6162	Philadelphia-Wilmington-Atlantic City, PA-NJ-DE-MD	Philadelphia	3	34.0
CMSA*	8872	Washington-Baltimore, DC-MD-VA-WV	Washington DC	2	27.2
MSA*	0520	Atlanta,GA	Atlanta	1	26.6
MSA*	1720	Colorado Springs,CO	Colorado Springs	69	34.8
MSA*	2320	El Paso,TX	El Paso	2	35.1
MSA	3600	Jacksonville,FL	Jacksonville	2	15.9
MSA*	4120	Las Vegas,NV-AZ	Las Vegas	11	27.1
MSA*	6200	Phoenix-Mesa,AZ	Phoenix	37	40.5
MSA	6520	Provo-Orem,UT	Provo	0	28.9
MSA*	7040	St, Louis,MO-IL	St. Louis	8	27.2
MSA/CMSA	-	Other MSA/CMSA	Other CMSA	10	31.9
-	-	Other Not MSA	Not MSA	2	19.7

[1] CMSA is consolidated metropolitan statistical area; MSA is metropolitan statistical area according to the 1999 Office of Management and Budget definitions (January 28, 2002 revision).
* Indicates locations that satisfied both the annual average and exceedance criteria.

7.2.3 Estimation of On-Road Concentrations using Ambient Concentrations

Since mobile sources can account for a large part of personal exposures to ambient NO_2 in some individuals, the potential impact of roadway levels of NO_2 was evaluated. A strong relationship has been reported between NO_2 levels measured on roadways and NO_2 measured at increasing distance from the road. This relationship has been described previously (e.g., Cape et al., 2004) using an exponential decay equation of the form:

$$C_x = C_b + C_v e^{-kx} \qquad \text{equation (7-1)}$$

where,

C_x = NO_2 concentration at a given distance (x) from a roadway (ppb)

C_b = NO_2 concentration (ppb) at a distance from a roadway, not directly influenced by road or non-road source emissions.

C_v = NO_2 concentration contribution from vehicles on a roadway (ppb)

k = Rate constant describing NO_2 combined formation/decay with perpendicular distance from roadway ($meters^{-1}$)

x = Distance from roadway (meters)

Based on the findings of several researchers, 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 10 meter 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 here as *on-road*, the equation reduces to the sum of the non-source influenced NO_2 concentration and the concentration contribution expected from vehicle emissions on the roadway using

$$C_r = C_a (1 + m) \qquad \text{equation (7-2)}$$

where,

C_r = 1-hour on-road NO_2 concentration (ppb)

C_a = 1-hour ambient monitoring NO_2 concentration (ppb) either *as is* or modified to just meet the current standard

m = Modification factor derived from estimates of C_v/C_b (from equation (7-1))

and assuming that $C_a = C_b$.[10]

[10] Note that C_a differs from C_b since C_a may include the influence of on-road as well as non-road sources. However, it is expected that for most monitors the influence of on-road emissions is minimal so that $C_a \cong C_b$.

To estimate on-road NO_2 levels as a function of the level recorded at ambient monitors and the distance of those monitors from a roadway, empirical data from published scientific literature were used. A literature review was conducted to identify published studies containing NO_2 concentrations on roadways and at varying distances from roadways. Relevant data identified from this literature review were used to estimate *m* (equation 7-1) generating a distribution of values for use in estimating on-road concentrations. See Appendix A, section 8 for a detailed explanation of derivation of the on-road modification factors and the literature sources used.

Theoretically, NO_2 concentrations can increase at a distance from the road due to chemical interaction of NO_x with O_3, the magnitude of which can be driven by certain meteorological conditions (e.g., wind direction). As such, the maximum NO_2 concentration may not occur on the road but at a distance from the road. However, there are two important components of this estimation procedure that need consideration. First, the relationship developed from peer-reviewed NO_2 roadway and near-road measurement studies was used to estimate NO_2 concentrations that occur on the road and not used to estimate NO_2 concentrations at a distance from the road. If this does occur in a location, the ambient monitors located within 100 m of a road would capture this potential effect, where such monitors are available. Second, since there is potential for monitors that are sited near roadways to be influenced by vehicle emissions and equation (7-2) assumes the ambient concentration is approximating NO_2 concentrations not directly influenced by the roadway, the monitors within 100 m were not used for calculating the on-road concentrations. The uncertainty regarding these issues and potential effect on exposure estimates are discussed in section 7.4.

To estimate NO_2 levels on roadways, each monitoring site was randomly assigned one on-road factor (*m*) for summer months and one for non-summer months from the derived empirical distribution. On-road factors were assigned randomly because we expect the empirical relationship between C_v and C_b to vary from place to place and we do not have sufficient information to match specific ratios with specific locations. Hourly NO_2 levels were estimated for each site-year of data in a location using equation (7-2) and the randomly assigned on-road modification factors. The process was simulated 100 times for each site-year of hourly data. For example, the Boston CMSA location had 210 random selections from the on-road distributions applied independently to the total site-years of data (105). Following 100 simulations, a total of

10,500 site-years of data were generated using this procedure (along with 21,000 randomly assigned on-road values selected from the appropriate empirical distribution).

Simulated on-road NO_2 concentrations were then used to generate concentration distributions for the annual average concentrations and distributions for the number of exceedances of short-term potential health effect benchmark levels. Mean and median values are reported to represent the central tendency of each parameter estimate. Since there were multiple site-years and numerous simulations performed at each location using all valid site-years of data, results for the upper percentiles were expanded to the 95th, 98th and 99th percentiles of the distribution. In using the Boston CMSA data as an example for years 1995-2000, 5800 site years of on-road concentration hourly data were simulated, and both the annual average concentration and numbers of exceedances of potential health effect benchmark levels were calculated. The 95th, 98th and 99th percentiles were the 5510th, the 5684th, and the 5742nd highest values, respectively, of the 5800 calculated and ranked values. Roadways with high vehicle densities are likely better represented by on-road concentration estimates at the upper tails of the distribution.

7.3 AIR QUALITY AND HEALTH RISK CHARACTERIZATION RESULTS

7.3.1 Ambient Air Quality (As Is)

As described earlier, this first scenario analyzing the *as is* air quality is based purely on the measurement data. The air quality data obtained from AQS were separated into two year-groups, one representing historic data (1995-2000) and the other representing more recent data (2001-2006). Detailed descriptive statistics regarding concentration distributions for particular locations, monitoring sites, and specific monitoring years are provided in the Appendix A, section 5. A summary of the descriptive statistics for the annual average ambient NO_2 concentrations at each selected location is provided in Tables 7-3 and 7-4 for monitors sited ≥100 m and < 100 m from a major road, respectively. None of the locations contained a measured exceedance of the current standard of 0.053 ppm at any monitor. The highest observed annual average concentrations were measured in Los Angeles and Phoenix during the historic monitoring period and considering the monitors ≥100 m from a major road. There were a fewer number of locations with monitors sited < 100 m of a major road, however in most of the locations where comparative monitoring data were available, the annual average concentrations

were greater at the monitors within 100 m of a major road (in 23 of 27 possible location/year-group combinations). Four locations (Denver, Los Angeles, Phoenix, St. Louis) contained higher concentrations at the more distant monitors for one year-group when compared with the monitors within 100 m. Where concentrations were greater at the near road monitors, the concentrations were on average about 20-25% higher when compared with the more distant monitors in each corresponding location, regardless of year-group. A comparison of the year-group of data within each monitor site-group indicates that the more recent monitoring concentrations were lower, on average by about 13-15%. These average trends in concentration across year-group and monitor site group were generally observed across all percentiles of the distribution.

Table 7-3. Monitoring site-years and annual average NO_2 concentrations for two monitoring periods, historic and recent air quality data (as is) using monitors sited ≥100 m of a major road.

	1995-2000							2001-2006						
	Site-	Annual Mean (ppb) [1]						Site-	Annual Mean (ppb) [1]					
Location	Years	mean	min	med	p95	p98	p99	Years	mean	min	med	p95	p98	p99
Boston	18	18	5	18	25	25	25	14	9	5	9	12	12	12
Chicago	28	20	9	22	27	28	28	17	21	16	19	28	28	28
Cleveland	5	19	17	20	21	21	21	3	18	17	17	19	19	19
Denver	7	22	15	23	26	26	26	5	21	18	21	26	26	26
Detroit	12	19	12	19	26	26	26	12	19	14	19	23	23	23
Los Angeles	92	27	6	28	40	46	46	105	20	5	20	33	34	36
Miami	9	9	9	9	10	10	10	10	8	7	8	10	10	10
New York	47	24	11	26	35	36	36	48	20	10	19	28	31	31
Philadelphia	35	21	15	20	33	33	33	26	19	14	18	28	28	28
Washington DC	33	18	9	19	25	26	26	35	17	7	18	24	25	25
Atlanta	24	14	5	15	25	27	27	29	12	3	14	19	23	23
Colorado Springs	25	16	7	17	24	35	35	-	-	-	-	-	-	-
El Paso	8	19	14	18	23	23	23	24	15	8	16	18	18	18
Jacksonville	6	15	14	15	16	16	16	4	14	13	14	15	15	15
Las Vegas	8	10	3	6	24	24	24	27	10	1	7	22	22	22
Phoenix	14	30	26	29	34	34	34	14	25	21	24	29	29	29
Provo	6	24	23	24	24	24	24	6	24	21	23	29	29	29
St. Louis	18	17	5	19	21	21	21	13	16	12	16	21	21	21
Other CMSA	1135	14	1	14	24	26	28	1177	12	1	12	20	22	24
Not MSA	200	8	0	7	16	19	19	243	7	1	6	14	16	16

[1] The mean is the sum of the annual means for each monitor in a particular location divided by the number of site-years across the monitoring period. The min, med, p95, p98, p99 represent the minimum, median, 95th, 98th, and 99th percentiles of the distribution for the annual mean.
[2] Colorado Springs monitoring data were collected as part of short-term study completed in September 2001, therefore there are no 2001-2006 data.

Table 7-4. Monitoring site-years and annual average NO_2 concentrations for two monitoring periods, historic and recent air quality data (as is) using monitors sited <100 m of a major road.

Location	1995-2000							2001-2006						
	Site-Years	Annual Mean (ppb) [1]						Site-Years	Annual Mean (ppb) [1]					
		mean	min	med	p95	p98	p99		mean	min	med	p95	p98	p99
Boston	40	18	6	20	31	31	31	33	18	7	18	25	30	30
Chicago	19	29	22	31	34	34	34	19	27	18	28	32	32	32
Cleveland	6	26	23	27	28	28	28	8	20	14	22	24	24	24
Denver	19	14	6	9	35	35	35	5	31	27	29	37	37	37
Los Angeles	101	25	4	23	45	46	46	72	25	4	27	37	40	41
Miami	15	11	6	9	17	17	17	10	10	6	10	16	16	16
New York	46	31	22	29	42	42	42	33	29	18	28	40	40	40
Philadelphia	11	30	26	29	34	34	34	13	23	18	24	30	30	30
Washington DC	36	23	13	23	27	27	27	31	20	13	20	26	26	26
Colorado Springs	1	18	18	18	18	18	18							
El Paso	6	29	23	29	35	35	35	6	18	13	19	22	22	22
Las Vegas	8	19	7	25	27	27	27	8	15	3	19	23	23	23
Phoenix	8	31	24	30	40	40	40	13	25	11	24	37	37	37
St, Louis	38	18	9	19	26	27	27	30	15	8	15	23	25	25

[1] The mean is the sum of the annual means for each monitor in a particular location divided by the number of site-years across the monitoring period. The min, med, p95, p98, p99 represent the minimum, median, 95th, 98th, and 99th percentiles of the distribution for the annual mean.
[2] Colorado Springs monitoring data were collected as part of short-term study completed in September 2001, therefore there are no 2001-2006 data.

The estimated number of exceedances of four potential health effect benchmark levels (150, 200, 250, and 300 ppb NO_2 for 1-hr) is shown in Tables 7-5 and 7-6 for the historic and recent ambient monitoring data, respectively, and where the monitors were sited ≥ 100 m from a major road. The number of exceedances of each benchmark were summed for the year at each monitor; a single monitor value of 10 could represent ten 1-hr exceedances that occurred in one day, 10 exceedances in 10 days, or some combination of multiple hours or days that totaled 10 exceedances for the year. In general, the number of benchmark exceedances was low across all locations and considering both year-groups of the *as is* air quality. The average number of exceedances of the lowest 1-hour concentration level of 150 ppb across each location was typically none or one. Considering that there are 8,760 hours in a year, this many exceedances amounts to a small fraction of the year (0.01%) containing an exceedance of the potential health effect benchmark level. For locations with greater than 1 yearly average exceedance, the numbers were primarily driven by a single site-year of data. For example, the Colorado Springs mean is 3 exceedances per year for the years 1995-2000; however, this mean was driven by a

single site-year that contained 69 exceedances of 200 ppb. That particular monitor (ID 0804160181) does not appear to have any unusual attributes (e.g., the closest major road is beyond a distance of 160 meters and the closest stationary source emitting > 5 tons per year (tpy) is at a distance > 4 km) except that a power generating utility (NAICS code 221112) located 7.2 km from the monitor has estimated emissions of 4,205 tpy. It is not known at this time whether this particular facility is influencing the observed concentration exceedances at this specific monitoring site. Similarly, Detroit contained the largest number of excedances of 200 ppb (a maximum of 12) for *as is* air quality data from years 2001-2006 (Table 7-6). Again, all of those exceedances occurred at one monitor (ID 2616300192) during one year (2002). The number of exceedances of higher potential benchmark concentration levels at each of the locations was less than that observed at the 200 ppb level. Most locations had no exceedances of 250 or 300 ppb, with higher numbers confined to the same aforementioned cities where exceedances of 200 ppb were observed.

When considering the historic data and monitors sited within 100 m of a major road (Table 7-7), a few locations contained exceedances of the potential health effect benchmark levels, driven mainly by observations from one or two monitors. For example, in Phoenix a single year from one monitor (ID 0401330031) was responsible for all observed exceedances of 200 ppb. This monitor is located 78 m from a major road along with 10 stationary sources located within 10 km of this monitor, 9 of which contained estimated emissions of less than 60 tpy (one source emitted 272 tpy, see Appendix A, section 4). It is not known if observed exceedances of 200 ppb at this monitor are a result of proximity of major roads or the stationary sources. There were fewer locations with observed exceedances of the benchmark levels at the monitors sited within 100 m of a major road considering the more recent *as is* air quality. Eleven of thirteen total locations contained an average of zero exceedances of the 150 ppb benchmark level (Table 7-8).

Table 7-5 Number of exceedances of short-term (1-hour) potential health effect benchmark levels in a year, 1995-2000 historic NO_2 air quality (as is) using monitors sited ≥100 m of a major road.

Location	Exceedances of 150 ppb [1]						Exceedances of 200 ppb [1]						Exceedances of 250 ppb [1]						Exceedances of 300 ppb [1]					
	mean	min	med	p95	P98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99
Boston	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chicago	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cleveland	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Denver	1	0	0	4	4	4	0	0	0	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Detroit	1	0	0	10	10	10	0	0	0	3	3	3	0	0	0	1	1	1	0	0	0	1	1	1
Los Angeles	3	0	0	22	42	44	0	0	0	2	2	4	0	0	0	0	1	2	0	0	0	0	0	1
Miami	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
New York	0	0	0	0	3	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Philadelphia	0	0	0	0	10	10	0	0	0	0	3	3	0	0	0	0	0	0	0	0	0	0	0	0
Washington DC	0	0	0	1	2	2	0	0	0	1	2	2	0	0	0	1	1	1	0	0	0	0	0	0
Atlanta	0	0	0	1	1	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Colorado Springs	8	0	0	47	143	143	3	0	0	3	69	69	1	0	0	0	23	23	0	0	0	0	4	4
El Paso	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Jacksonville	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Las Vegas	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Phoenix	0	0	0	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Provo	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
St. Louis	1	0	0	12	12	12	0	0	0	8	8	8	0	0	0	4	4	4	0	0	0	0	0	0
Other CMSA	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Not MSA	0	0	0	0	2	4	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0

Notes:
[1] The mean number of exceedances represents the number of exceedances occurring at all monitors in a particular location divided by the number of site-years across the monitoring period. The min, med, p95, p98, and p99 represent the minimum, median, 95th, 98th, and 99th percentiles of the distribution for the number of exceedances in any one year within the monitoring period.

Table 7-6 Number of exceedances of short-term (1-hour) potential health effect benchmark levels in a year, 2001-2006 recent NO_2 air quality (as is) using monitors sited ≥100 m of a major road.

Location	Exceedances of 150 ppb [1]						Exceedances of 200 ppb [1]						Exceedances of 250 ppb [1]						Exceedances of 300 ppb [1]					
	mean	min	med	p95	P98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99
Boston	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chicago	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cleveland	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Denver	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Detroit	2	0	0	16	16	16	1	0	0	12	12	12	1	0	0	8	8	8	0	0	0	5	5	5
Los Angeles	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Miami	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
New York	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Philadelphia	0	0	0	0	1	1	0	0	0	0	1	1	0	0	0	0	1	1	0	0	0	0	0	0
Washington DC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Atlanta	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
El Paso	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Jacksonville	2	0	1	6	6	6	1	0	1	2	2	2	0	0	0	1	1	1	0	0	0	0	0	0
Las Vegas	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Phoenix	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Provo	7	0	0	39	39	39	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
St. Louis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other CMSA	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Not MSA	0	0	0	0	1	2	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0

Notes:

[1] The mean number of exceedances represents the number of exceedances occurring at all monitors in a particular location divided by the number of site-years across the monitoring period. The min, med, p95, p98, and p99 represent the minimum, median, 95th, 98th, and 99th percentiles of the distribution for the number of exceedances in any one year within the monitoring period.

[2] Colorado Springs monitoring data were collected as part of short-term study completed in September 2001, therefore there are no 2001-2006 data.

Table 7-7. Number of exceedances of short-term (1-hour) potential health effect benchmark levels in a year, 1995-2000 historic NO_2 air quality (as is) using monitors sited <100 m of a major road.

Location	Exceedances of 150 ppb [1]						Exceedances of 200 ppb [1]						Exceedances of 250 ppb [1]						Exceedances of 300 ppb [1]					
	mean	min	med	p95	P98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99
Boston	0	0	0	0	1	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Chicago	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cleveland	2	0	0	9	9	9	0	0	0	1	1	1	0	0	0	1	1	1	0	0	0	0	0	0
Denver	0	0	0	6	6	6	0	0	0	1	1	1	0	0	0	1	1	1	0	0	0	0	0	0
Los Angeles	2	0	0	11	18	33	0	0	0	1	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Miami	0	0	0	3	3	3	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
New York	0	0	0	2	3	3	0	0	0	0	3	3	0	0	0	0	0	0	0	0	0	0	0	0
Philadelphia	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Washington DC	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Colorado Springs	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
El Paso	2	0	1	7	7	7	0	0	0	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Las Vegas	1	0	0	11	11	11	1	0	0	11	11	11	0	0	0	3	3	3	0	0	0	3	3	3
Phoenix	27	0	1	147	147	147	5	0	0	37	37	37	0	0	0	3	3	3	0	0	0	0	0	0
St, Louis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Notes:
[1] The mean number of exceedances represents the number of exceedances occurring at all monitors in a particular location divided by the number of site-years across the monitoring period. The min, med, p95, p98, and p99 represent the minimum, median, 95th, 98th, and 99th percentiles of the distribution for the number of exceedances in any one year within the monitoring period.

Table 7-8. Number of exceedances of short-term (1-hour) potential health effect benchmark levels in a year, 2001-2006 recent NO_2 air quality (as is) using monitors sited <100 m of a major road.

Location	Exceedances of 150 ppb [1]						Exceedances of 200 ppb [1]						Exceedances of 250 ppb [1]						Exceedances of 300 ppb [1]					
	mean	min	med	p95	P98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99
Boston	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chicago	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cleveland	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Denver	1	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Los Angeles	0	0	0	2	2	6	0	0	0	0	1	1	0	0	0	0	1	1	0	0	0	0	0	0
Miami	1	0	0	5	5	5	0	0	0	3	3	3	0	0	0	3	3	3	0	0	0	3	3	3
New York	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Philadelphia	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Washington DC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
El Paso	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Las Vegas	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Phoenix	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
St, Louis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Notes:
[1] The mean number of exceedances represents the number of exceedances occurring at all monitors in a particular location divided by the number of site-years across the monitoring period. The min, med, p95, p98, and p99 represent the minimum, median, 95th, 98th, and 99th percentiles of the distribution for the number of exceedances in any one year within the monitoring period.

7.3.2 On-Road Concentrations Derived From Ambient Air Quality (As Is)

Descriptive statistics for estimated on-road NO_2 concentrations are presented in Table 7-9. These estimated on-road concentrations were generated using the simulation procedure described above (section 7.2.3) and represent the second scenario. For the 18 named locations, the calculation only used monitors sited at a distance ≥ 100 m of a major road. The two grouped locations (i.e., "Other CMSA" and "Not MSA") did not have estimated monitor distances to major roads therefore all monitoring data available were used to estimate the distribution of on-road NO_2 concentrations.

The simulated on-road annual average NO_2 concentrations are, on average, a factor of 1.8 higher than their respective ambient levels. This falls within the range of ratios reported in the ISA (about 2-fold higher concentrations on roads) (ISA, section 2.5.4). Los Angeles, New York, and Phoenix were predicted to have the highest on-road NO_2 levels. This is a direct result of these locations already containing some of the highest "*as-is"* NO_2 concentrations prior to the on-road simulation (see Table 7-3).

The median of the simulated concentration estimates for Los Angeles were compared with NO_2 measurements provided by Westerdahl et al. (2005) for arterial roads and freeways in the same general location during spring 2003. Although the averaging time is not exactly the same, comparison of the medians is judged to be appropriate.[11] The estimated median on-road concentration for 2001-2006 is 36 ppb which falls within the range of 31 ppb to 55 ppb identified by Westerdahl et al. (2005).

On average, most locations are predicted to have fewer than 10 exceedances per year for the 200 ppb potential health effect benchmark while the median frequency of exceedances in most locations is estimated to be 1 or less per year (Tables 7-10 and 7-11). When considering the lower 1-hour benchmark of 150 ppb, most locations (17 out of 20) were estimated to have less than 50/year, on average. There are generally fewer predicted mean exceedances of the potential health effect benchmark levels when considering recent air quality compared with the historic air quality. Areas with a relatively high number of estimated exceedances (e.g., Provo) are likely influenced by the presence of a small number of monitors and one or a few exceptional

[11] Table 10 considers annual average of hourly measurements while Westerdahl et al. (2005) reported between 2 to 4 hour average concentrations. Over time, the mean of 2-4 hour averages will be similar to the mean of hourly concentrations, with the main difference being in the variability (and hence the various percentiles of the distribution outside the central tendency).

site-years where there were unusually high concentrations at the upper percentiles of the concentration distribution.

The upper percentiles for estimated number of exceedances of the 150 ppb, 1-hr average level in most locations using the historic ambient monitoring data was between 100 and 300 per year, while a few locations were estimated to contain up to a several hundred exceedances (e.g., Los Angeles, New York, and Phoenix). There were lower numbers of estimated exceedances considering the 2001-2006 air quality compared with the historic data, with most locations containing under 200 estimated exceedances of 150 ppb per year at the 98^{th} and 99^{th} percentiles. As expected, the frequency of benchmark exceedances at all locations was lower when considering any of the higher benchmark levels (i.e., 200, 250, 300 ppb, 1-hr average) compared with 150 ppb.

The number of predicted benchmark exceedances across large urban areas may be used to broadly represent particular locations within those types of areas. For example, Chicago, New York, and Los Angeles are large CMSAs, have several monitoring sites, and have a large number of roadways. Each of these locations was estimated to have, on average, about 10 exceedances of 200 ppb per year on-roads. Assuming that the on-road exceedances distribution generated from the existing monitoring is proportionally representing the distribution of roadways within each location, about one-half of the roads in these areas would not have any on-road concentrations in excess of 200 ppb. This is because the median value for exceedances of 200 ppb in most locations was estimated as zero. However, Tables 7-10 and 7-11 indicate that there is also a possibility of tens to just over a hundred exceedances of 200 ppb in a year as an upper bound estimate on certain roads/sites in a particular year.

Table 7-9. Estimated annual average on-road NO_2 concentrations for two monitoring periods, historic and recent air quality data (as is).

Location	1995-2000							2001-2006						
	Site-Years	Annual Mean (ppb) [1]						Site-Years	Annual Mean (ppb) [1]					
		mean	min	med	p95	p98	p99		mean	min	med	p95	p98	p99
Boston	1800	32	7	32	51	55	57	1400	16	7	16	25	28	29
Chicago	2800	37	11	39	59	63	66	1700	37	20	35	57	64	66
Cleveland	500	35	22	34	47	49	53	300	32	22	32	42	43	45
Denver	700	39	19	38	55	58	62	500	39	23	38	54	61	62
Detroit	1200	35	15	34	52	57	59	1200	34	18	34	47	52	54
Los Angeles	9200	50	8	49	83	91	97	10500	37	6	36	63	72	77
Miami	900	17	11	17	23	25	26	1000	15	9	14	21	24	24
New York	4700	43	14	42	73	78	83	4800	35	12	34	56	62	66
Philadelphia	3500	39	19	36	63	73	77	2600	34	18	32	52	60	64
Washington	3300	33	12	33	53	58	61	3500	31	9	31	51	56	59
Atlanta	2400	26	6	25	49	57	60	2900	21	4	23	40	43	47
Colorado Springs[2]	2500	30	9	30	52	64	73	-	-	-	-	-	-	-
El Paso	800	34	17	33	49	54	57	2400	26	10	26	39	43	43
Jacksonville	600	28	18	27	37	39	41	400	25	17	25	34	36	37
Las Vegas	800	17	4	11	45	50	55	2700	18	2	13	43	46	50
Phoenix	1400	54	33	52	75	78	80	1400	45	26	43	63	70	72
Provo	600	43	29	42	58	62	64	600	43	26	41	61	69	70
St. Louis	1800	31	7	33	47	50	52	1300	30	16	29	41	46	49
Other CMSA	113500	26	1	25	47	53	57	117700	21	1	21	39	45	48
Not MSA	20000	14	0	12	31	35	39	24300	12	1	11	27	31	33

[1] The mean is the sum of the annual means for each monitor in a particular location divided by the number of site-years across the monitoring period. The min, med, p95, p98, p99 represent the minimum, median, 95th, 98th, and 99th percentiles of the distribution for the annual mean.

[2] Colorado Springs monitoring data were collected as part of short-term study completed in September 2001, therefore there are no 2001-2006 data.

Table 7-10. Estimated number of exceedances of short-term (1-hour) potential health effect benchmark levels in a year on-roads, 1995-2000 historic NO_2 air quality (as is).

Location	Exceedances of 150 ppb [1]						Exceedances of 200 ppb [1]						Exceedances of 250 ppb [1]						Exceedances of 300 ppb [1]					
	mean	min	med	p95	P98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99
Boston	11	0	1	79	106	125	1	0	0	9	20	24	0	0	0	1	4	7	0	0	0	0	1	1
Chicago	39	0	2	212	338	385	7	0	0	41	97	118	1	0	0	6	23	30	0	0	0	0	3	7
Cleveland	15	0	1	108	130	146	2	0	0	19	27	31	0	0	0	1	5	5	0	0	0	1	1	1
Denver	48	0	17	185	230	288	8	0	4	36	46	53	2	0	1	10	12	15	1	0	0	4	6	7
Detroit	39	0	19	158	207	270	10	0	2	48	72	86	4	0	1	21	34	35	2	0	0	14	21	26
Los Angeles	166	0	54	738	1023	1268	43	0	6	213	348	508	12	0	0	63	118	188	4	0	0	17	39	68
Miami	3	0	0	13	27	27	0	0	0	2	4	5	0	0	0	0	0	1	0	0	0	0	0	0
New York	63	0	8	397	560	685	13	0	0	92	155	212	3	0	0	21	44	55	1	0	0	4	10	14
Philadelphia	25	0	2	124	311	369	4	0	0	20	45	63	1	0	0	4	11	15	0	0	0	0	5	7
Washington DC	21	0	1	128	208	240	3	0	0	20	39	56	1	0	0	2	8	11	0	0	0	1	2	3
Atlanta	24	0	1	160	271	357	4	0	0	31	57	87	1	0	0	3	11	21	0	0	0	1	1	2
Colorado Springs	45	0	0	267	447	626	21	0	0	171	264	325	12	0	0	111	183	219	7	0	0	55	121	160
El Paso	21	0	8	96	141	149	4	0	0	20	31	39	1	0	0	5	7	8	0	0	0	0	2	2
Jacksonville	3	0	0	13	30	36	0	0	0	1	2	4	0	0	0	0	1	1	0	0	0	0	0	0
Las Vegas	14	0	0	95	294	306	2	0	0	5	34	36	0	0	0	0	6	6	0	0	0	0	0	0
Phoenix	104	0	31	447	630	670	14	0	2	65	89	102	2	0	0	13	21	27	1	0	0	3	6	11
Provo	21	0	0	112	195	245	2	0	0	9	33	34	0	0	0	0	1	4	0	0	0	0	0	0
St, Louis	14	0	0	74	121	132	2	0	0	15	25	28	1	0	0	10	13	14	1	0	0	7	11	13
Other MSA/CMSA	10	0	0	55	109	168	1	0	0	6	18	32	0	0	0	1	3	6	0	0	0	0	1	2
Other Not MSA	2	0	0	11	31	55	1	0	0	2	7	14	0	0	0	1	2	4	0	0	0	0	1	2

Notes:
[1] The mean number of exceedances represents the number of exceedances occurring at all monitors in a particular location divided by the number of site-years across the monitoring period. The min, med, p95, p98, and p99 represent the minimum, median, 95th, 98th, and 99th percentiles of the distribution for the number of exceedances in any one year within the monitoring period.

Table 7-11. Estimated number of exceedances of short-term (1-hour) potential health effect benchmark levels in a year on-roads, 2001-2006 recent NO_2 air quality (as is).

Location[2]	Exceedances of 150 ppb [1]						Exceedances of 200 ppb [1]						Exceedances of 250 ppb [1]						Exceedances of 300 ppb [1]					
	mean	min	med	p95	P98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99	mean	min	med	p95	p98	p99
Boston	0	0	0	1	2	10	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Chicago	24	0	1	160	211	337	4	0	0	17	44	69	0	0	0	1	5	10	0	0	0	0	1	1
Cleveland	14	0	3	79	89	89	2	0	0	16	23	23	0	0	0	4	5	6	0	0	0	2	3	3
Denver	41	0	6	171	270	379	4	0	0	25	40	53	0	0	0	3	6	7	0	0	0	0	1	1
Detroit	20	0	3	116	149	171	5	0	0	29	44	45	2	0	0	16	22	28	1	0	0	13	14	21
Los Angeles	42	0	4	227	405	546	7	0	0	37	87	129	1	0	0	7	20	28	0	0	0	1	3	10
Miami	1	0	0	4	9	16	0	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0
New York	21	0	1	129	210	280	3	0	0	22	45	72	1	0	0	3	10	16	0	0	0	0	1	2
Philadelphia	12	0	1	62	110	211	1	0	0	5	12	30	0	0	0	1	1	7	0	0	0	0	1	1
Washington DC	11	0	0	81	130	141	1	0	0	7	14	21	0	0	0	0	1	2	0	0	0	0	0	0
Atlanta	8	0	0	52	101	121	1	0	0	8	16	25	0	0	0	1	3	6	0	0	0	0	1	2
El Paso	6	0	0	34	45	54	1	0	0	4	8	9	0	0	0	1	1	1	0	0	0	0	0	0
Jacksonville	7	0	2	29	53	53	3	0	1	15	23	24	2	0	0	8	15	15	1	0	0	5	8	8
Las Vegas	9	0	0	39	169	205	1	0	0	3	14	15	0	0	0	0	0	2	0	0	0	0	0	0
Phoenix	37	0	2	184	302	350	3	0	0	14	28	44	0	0	0	1	3	4	0	0	0	0	0	0
Provo	117	0	1	658	702	703	70	0	0	547	662	662	33	0	0	234	606	612	13	0	0	3	423	435
St, Louis	7	0	0	48	84	102	1	0	0	3	10	14	0	0	0	0	2	2	0	0	0	0	0	1
Other MSA/CMSA	4	0	0	17	44	76	0	0	0	1	5	10	0	0	0	0	1	1	0	0	0	0	0	0
Other Not MSA	1	0	0	4	14	27	0	0	0	1	4	8	0	0	0	0	2	3	0	0	0	0	1	2

Notes:

[1] The mean number of exceedances represents the number of exceedances occurring at all monitors in a particular location divided by the number of site-years across the monitoring period. The min, med, p95, p98, and p99 represent the minimum, median, 95th, 98th, and 99th percentiles of the distribution for the number of exceedances in any one year within the monitoring period.

[2] Colorado Springs monitoring data were collected as part of short-term study completed in September 2001, therefore there are no 2001-2006 data.

7.3.3 Ambient Air Quality Adjusted to Just Meet the Current and Alternative Standards

As described in section 6.2, each of the current and alternative standards were evaluated using the more recent air quality data set (i.e., 2001-2006). Analysis results are presented for a few selected locations, potential health effect benchmarks, and alternative standard levels, since there were a total of 10 air quality scenarios (8 alternative standards, the current standard, and as is), for each year group of data (2001-2003 and 2004-2006), for each of the monitor groups (<100m and ≥100 m), and evaluated at 5 potential health effect benchmark levels (100, 150, 200, 250, 300 ppb 1-hour). All of the results for each location are provided in Appendix A, section 9, much of which is summarized here in a series of key figures.

Figure 7-1 illustrates the estimated mean number of exceedances of the lowest concentration levels (i.e., 100, 150, and 200 ppb) for each year-group air quality data adjusted to just meeting the current annual average standard. The number of estimated exceedances of 100 ppb generally ranges from tens to several hundred, with subtle differences in the estimates for each year-group and monitor siting category. For many of the locations, estimated number of exceedances of 100 ppb are slightly higher for the 2004-2006 year-group when compared with the 2001-2003 year-group, and the monitors sited at ≥100 m from a major road contained more estimated exceedances that the monitors sited within 100 m of a major road. The estimated number of exceedances of 150 and 200 ppb were much lower, for most locations the average number of exceedances was under 100. Trends noted for these concentration levels were consistent with that estimated for the 100 ppb level, with the lowest number of estimated exceedances of 150 and 200 ppb associated with the 2001-2003 air quality for monitors < 100 m of a major road. Note however that thirty-two of the 63 possible year-group and monitor-site data combinations at the 19 locations did not have any exceedances of the 200 ppb level.

Figure 7-2 presents the mean estimated number of exceedances when considering the air quality adjusted to just meeting the potential alternative standard levels, using Chicago as an example to illustrate the relationship between the two forms of the standard. The trends in the results presented for Chicago that apply to the other locations with a few exceptions. As expected, the estimated number of exceedances is lower for a 99th percentile form compared with each corresponding level using the 98th percentile form of alternative standard. In general, the

number of estimated exceedances of the potential health effect benchmark levels at monitoring sites < 100 m from a major road is greater than the numbers estimated for monitors sited ≥ 100 m from a major road. This is what one would expect given the greater potential for vehicle emissions influencing ambient concentrations at near road monitors. As expected, the number of exceedances of the potential health effect benchmark levels decreases with decreasing alternative standard level. Regardless of year-group or monitoring group, an alternative standard level of 100 ppb tended to reduce the number of estimated exceedances to either a few to none.

Figure 7-3 presents mean estimated number of exceedances of the 200 ppb concentration level for a few additional locations, Phoenix, Los Angeles, Philadelphia, and St. Louis. Again, there are trends in these results that are consistent with that reported for the Chicago results, with few exceptions. For example, in St. Louis the estimated number of exceedances at monitors located ≥ 100 m from a major road were greater than those estimated using the monitoring sites < 100 m from a major road. Also note that there were variable results when comparing year-groups across the different locations within the monitor site-group; sometimes the year 2001-2003 contained greater numbers of exceedances when compared with 2004-2006, other time not. However, the alternative standard level of 100 ppb at either percentile consistently reduced the number of benchmark exceedances.

Tables 7-12 and 7-13 summarize the annual mean concentrations and estimated number of exceedances given 2001-2003 air quality adjusted that just meets the 1-hour 100 ppb 98th percentile standard at monitors sited ≥ 100 m and < 100 m from a major road, respectively. The tables provide a more comprehensive comparison of the numbers of exceedances of the complete range of potential health effect benchmarks for each of the locations, as well as providing upper percentile estimates for each of the parameters. These particular results are provided to describe trends within a given standard level, similar results are expected with differing year-group. The complete results for all of the standard levels, including the observed number of exceedances (*as is* air quality) provided in Appendix A, section 9. Most locations contained a mean of less than 100 exceedances of the 100 ppb concentration level, with upper percentile estimates ranging from the tens to a few hundred. These results are comparably less than those estimated using air quality adjusted to just meeting the current standard (Figure 7-1). At potential health effect benchmark levels above 100 ppb, there were few estimated exceedances, particularly at and above the 200 ppb level, considering both the mean and the upper percentiles.

Tables 7-14 summarizes the observed and estimated mean numbers of exceedances of 100 ppb using the 2001-2003 air quality *as is* and adjusted to just meeting the current standard and the potential alternative 98th percentile standards at each location. The number of exceedances for the as is air quality generally fell within the number of exceedances estimated using alternative 1-hour 98th percentile standards of 50 ppb and 100 ppb at each location. When the air quality was adjusted to just meeting the current annual average standard, the estimated number of exceedances fell within the range of that estimated using the alternative 1-hour 98th percentile standards of 100 ppb and 150 ppb at each location. In a similar manner, Table 7-15 summarizes the observed and estimated mean numbers of exceedances of 150 ppb 1-hour at each location. The number of exceedances using as is air quality in each location was most similar to that estimated using the alternative 1-hour 98th percentile standard of 50 ppb, while estimates using the air quality adjusted to just meeting the current standard again fell within the range of estimated numbers of exceedance using the alternative 1-hour 98th percentile standards of 100 ppb and 150 ppb at each location.

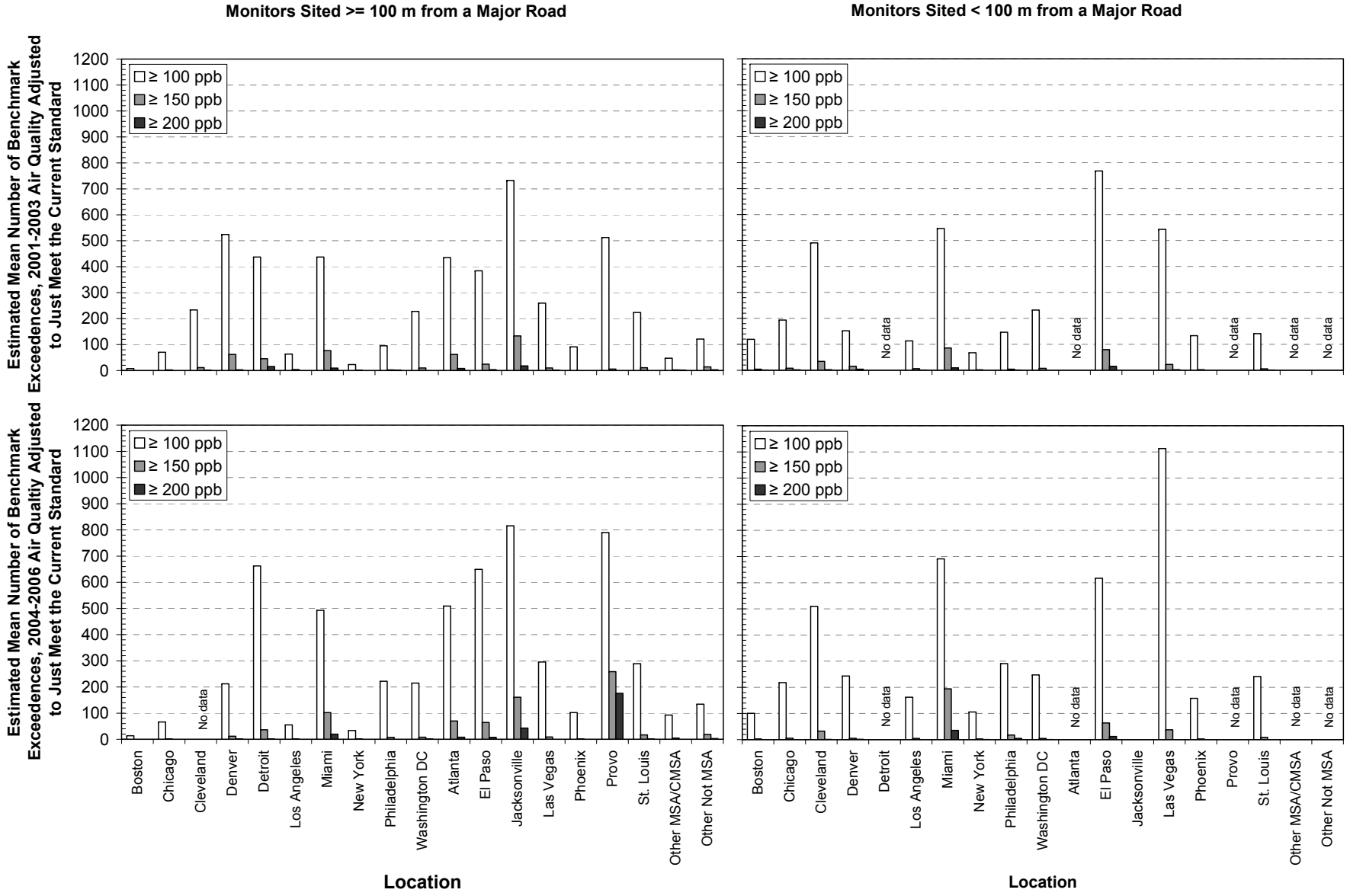


Figure 7-1. Estimated mean number of exceedances of selected 1-hour potential health effect benchmark levels, using recent air quality adjusted to just meeting the current annual standard (0.053 ppm). (Top row contains 2001-2003 air quality, bottom row contains 2004-2006 air quality. Left column contains monitors sited ≥ 100 m of a major road, right column contains monitors sited < 100 m of a road.)

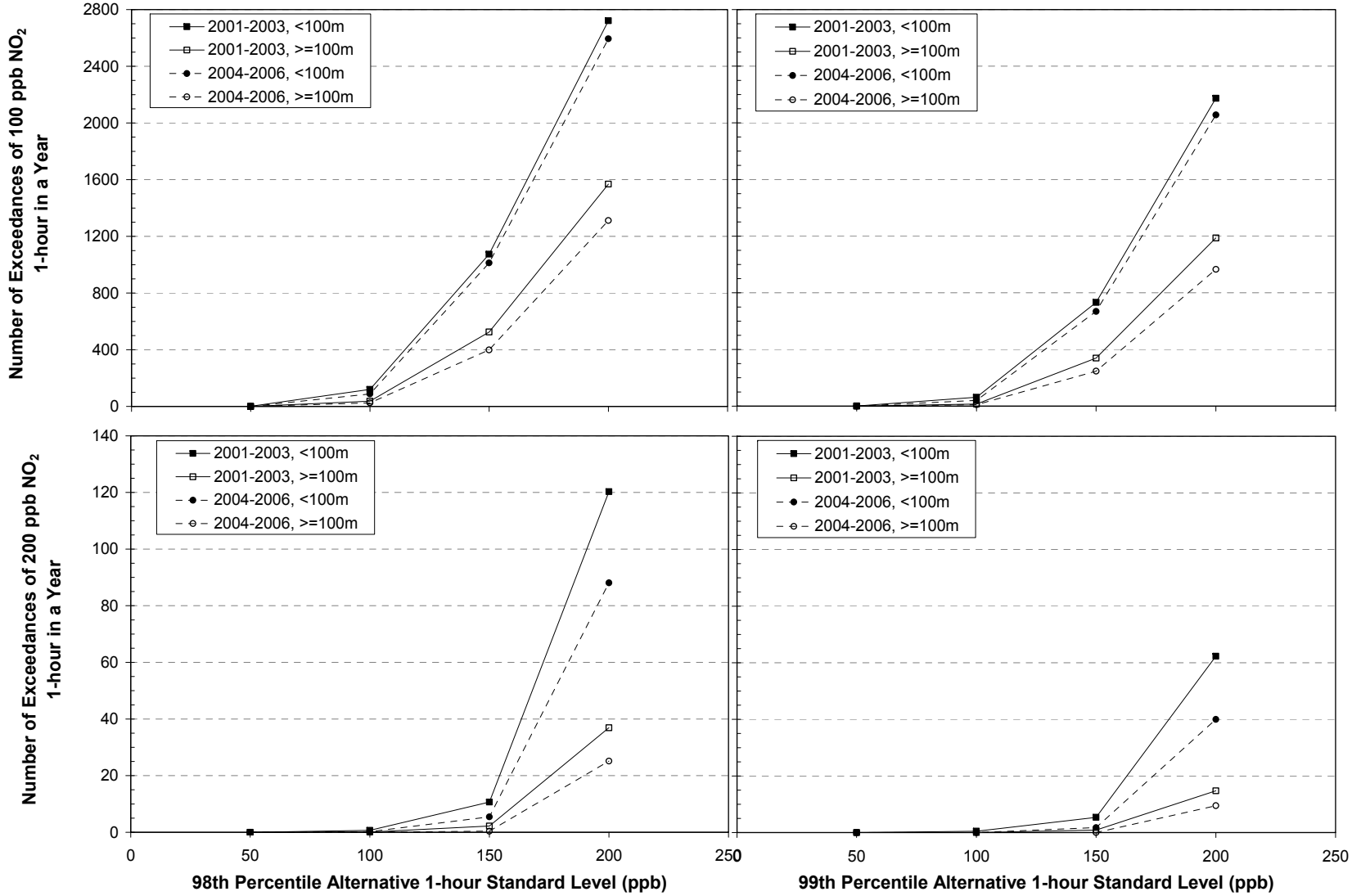


Figure 7-2. Estimated number of exceedances of potential health effect benchmarks (100 ppb, top; 200 ppb, bottom) in Chicago given just meeting alternative 1-hour standard levels (98th percentile, left; and 99th percentile, right) using recent air quality data from monitors sited < 100 m of a major road and sited ≥100 m of major roads.

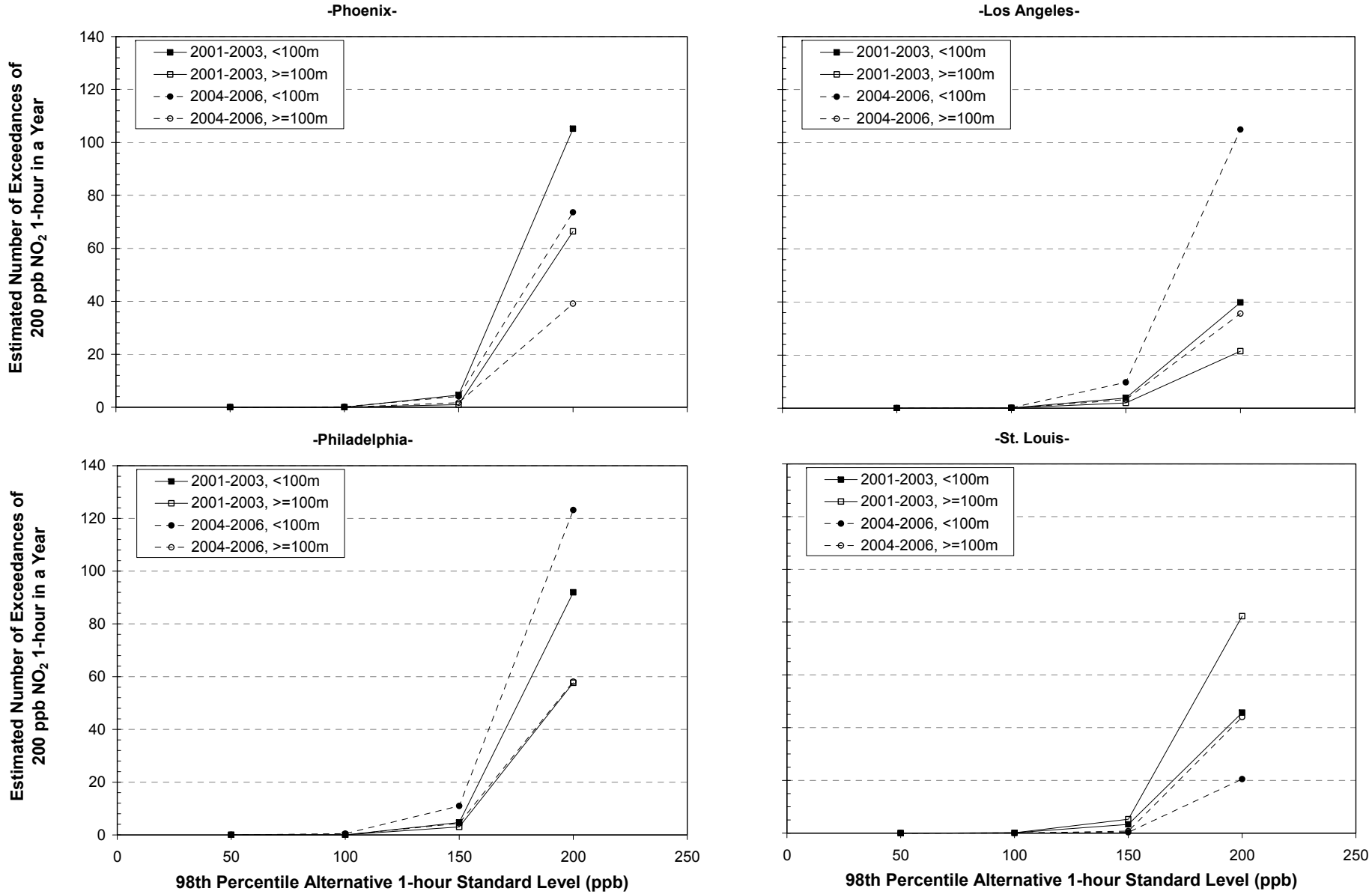


Figure 7-3. Estimated number of exceedances of 200 ppb in four locations (Phoenix, Los Angeles, Philadelphia, and St. Louis) given just meeting alternative 1-hour 98th percentile standard levels using recent air quality data from monitors sited < 100 m of a major road and sited ≥100 m of major roads.

Table 7-12 Estimated annual mean NO2 concentration and the number of exceedances of 1-hour NO2 concentration levels, using 2001-2003 air quality adjusted to just meeting a 1-hour 100 ppb 98th percentile alternative standard, monitoring locations sited ≥ 100 m of a major road.

Location	Site-Years	Annual Mean (ppb)				Number of Exceedances of 1-Hour Level																			
						≥ 100 ppb				≥ 150 ppb				≥ 200 ppb				≥ 250 ppb				≥ 300 ppb			
		Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99
Boston	6	18	10	21	22	4	0	2	18	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
Chicago	9	33	26	31	43	37	1	17	160	1	0	0	5	0	0	0	1	0	0	0	0	0	0	0	0
Cleveland	3	35	34	34	36	72	49	75	92	2	1	2	3	0	0	0	1	0	0	0	0	0	0	0	0
Denver	2	35	32	35	38	58	54	58	61	2	1	2	2	1	0	1	1	0	0	0	0	0	0	0	0
Detroit	6	40	36	39	45	146	88	140	217	18	1	7	47	8	0	3	30	5	0	1	25	3	0	1	15
Los Angeles	51	26	6	28	43	21	0	9	112	1	0	0	13	0	0	0	5	0	0	0	2	0	0	0	0
Miami	6	22	17	23	26	85	5	43	243	6	0	4	18	1	0	0	2	0	0	0	0	0	0	0	0
New York	26	29	16	27	45	19	0	9	89	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0
Philadelphia	14	34	25	32	50	58	4	33	244	1	0	1	3	0	0	0	1	0	0	0	1	0	0	0	1
Washington DC	18	34	16	39	46	93	0	71	274	3	0	1	10	0	0	0	0	0	0	0	0	0	0	0	0
Atlanta	14	22	7	27	41	61	0	17	335	3	0	0	23	0	0	0	3	0	0	0	1	0	0	0	1
El Paso	12	28	20	30	34	50	13	40	94	2	0	1	10	0	0	0	1	0	0	0	1	0	0	0	0
Jacksonville	2	36	36	36	37	160	124	160	195	10	4	10	15	1	0	1	2	1	0	1	2	1	0	1	2
Las Vegas	16	19	4	14	41	37	0	2	172	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0
Phoenix	5	39	32	42	43	66	8	91	115	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Provo	3	47	43	48	49	175	66	206	253	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
St. Louis	9	35	29	34	41	82	6	32	214	2	0	0	9	0	0	0	1	0	0	0	0	0	0	0	0
Other MSA/CMSA	612	16	1	17	31	2	0	0	24	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0
Other Not MSA	127	13	2	12	33	9	0	0	180	1	0	0	25	1	0	0	7	0	0	0	6	0	0	0	1

Table 7-13. Estimated annual mean NO_2 concentration and the number of exceedances of 1-hour NO_2 concentration levels, using 2001-2003 air quality adjusted to just meeting a 1-hour 100 ppb 98th percentile alternative standard, monitoring locations sited < 100 m of a major road.

Location[1]	Site-Years	Annual Mean NO_2 (ppb)				Number of Exceedances of 1-Hour Level																			
						≥ 100 ppb				≥ 150 ppb				≥ 200 ppb				≥ 250 ppb				≥ 300 ppb			
		Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99
Boston	19	34	13	39	57	67	0	44	221	2	0	0	8	0	0	0	1	0	0	0	0	0	0	0	0
Chicago	10	42	34	45	50	120	20	112	267	4	0	1	37	1	0	0	7	0	0	0	0	0	0	0	0
Cleveland	3	44	42	43	46	165	127	144	224	8	5	6	12	0	0	0	0	0	0	0	0	0	0	0	0
Denver	2	53	52	53	55	171	104	171	237	17	8	17	26	5	1	5	8	0	0	0	0	0	0	0	0
Los Angeles	44	30	5	31	48	40	0	25	160	1	0	0	8	0	0	0	3	0	0	0	1	0	0	0	1
Miami	6	26	15	25	40	103	34	81	252	4	0	1	17	0	0	0	2	0	0	0	0	0	0	0	0
New York	20	43	30	41	58	74	4	50	277	2	0	0	18	0	0	0	2	0	0	0	0	0	0	0	0
Philadelphia	7	43	33	42	53	92	14	67	230	2	0	2	3	0	0	0	0	0	0	0	0	0	0	0	0
Washington DC	14	39	26	42	48	92	0	87	197	1	0	0	6	0	0	0	1	0	0	0	0	0	0	0	0
El Paso	3	39	37	40	40	158	117	131	226	13	5	16	17	0	0	0	0	0	0	0	0	0	0	0	0
Las Vegas	6	26	6	28	42	89	0	81	196	2	0	0	12	0	0	0	0	0	0	0	0	0	0	0	0
Phoenix	5	44	31	50	54	105	1	135	201	1	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0
St. Louis	17	31	17	33	49	46	0	25	202	2	0	0	11	0	0	0	1	0	0	0	0	0	0	0	0

[1] Detroit, Atlanta, and Provo did not have any monitors sited within 100 m of a major road. The Other CMSA/MSA and Other Not MSA locations did not have estimated distances of monitors to major roads.

Table 7-14. Estimated mean number of exceedances of 100 ppb 1-hour NO_2 concentrations, using 2001-2003 air quality as is and that adjusted to just meeting the current and alternative standards (98th percentile) for monitoring locations sited ≥ 100 m and < 100 m of a major road.

	Sites >= 100 m of a major road						Sites < 100 m of a major road					
			Alternative 1-hour 98th percentile standard						Alternative 1-hour 98th percentile standard			
Location	As is	Current std	50	100	150	200	As is	Current std	50	100	150	200
Boston	0	8	0	4	163	546	0	119	0	67	812	1863
Chicago	1	71	0	37	525	1568	4	194	1	120	1075	2721
Cleveland	0	233	0	72	674	1707	0	491	0	165	1241	2865
Denver	2	525	1	58	932	2318	19	152	5	171	1836	4161
Detroit	9	438	8	146	1058	2461						
Los Angeles	7	63	0	21	241	914	13	113	0	40	403	1403
Miami	0	438	1	85	454	1044	0	546	0	103	566	1214
New York	1	23	0	19	331	1299	3	67	0	74	999	2837
Philadelphia	0	95	0	58	777	2041	0	146	0	92	1278	2873
Washington DC	0	228	0	93	896	1974	0	232	0	92	1061	2476
Atlanta	1	434	0	61	429	924						
El Paso	0	385	0	50	622	1553	2	768	0	158	1112	2330
Jacksonville	1	732	1	160	821	1770						
Las Vegas	0	260	0	37	533	1152	0	543	0	89	1038	1825
Phoenix	0	91	0	66	1064	2582	2	133	0	105	1681	3238
Provo	0	512	0	175	2187	3660						
St. Louis	0	223	0	82	798	1941	0	141	0	46	570	1687
Other MSA/CMSA	0	48	0	2	42	240						
Other Not MSA	1	121	1	9	77	284						

Table 7-15. Estimated mean number of exceedances of 150 ppb 1-hour NO_2 concentrations, using 2001-2003 air quality as is and that adjusted to just meeting the current and alternative standards (98th percentile) for monitoring locations sited ≥ 100 m and < 100 m of a major road.

	Sites >= 100 m of a major road						Sites < 100 m of a major road					
			Alternative 1-hour 98th percentile standard						Alternative 1-hour 98th percentile standard			
Location	As is	Current std	50	100	150	200	As is	Current std	50	100	150	200
Boston	0	0	0	0	4	56	0	4	0	2	67	431
Chicago	0	2	0	1	37	301	0	8	0	4	120	660
Cleveland	0	11	0	2	72	398	0	34	0	8	165	768
Denver	0	62	0	2	58	465	1	16	0	17	171	1015
Detroit	3	45	3	18	146	664						
Los Angeles	0	4	0	1	21	129	0	6	0	1	40	225
Miami	0	76	0	6	85	315	0	86	0	4	103	401
New York	0	1	0	0	19	177	0	2	0	2	74	589
Philadelphia	0	2	0	1	58	399	0	4	0	2	92	679
Washington DC	0	10	0	3	93	514	0	7	0	1	92	589
Atlanta	0	62	0	3	61	266						
El Paso	0	25	0	2	50	322	0	79	0	13	158	686
Jacksonville	1	134	1	10	160	585						
Las Vegas	0	10	0	0	37	288	0	22	0	2	89	615
Phoenix	0	0	0	0	66	617	0	2	0	1	105	996
Provo	0	5	0	1	175	1476						
St. Louis	0	11	0	2	82	470	0	6	0	2	46	309
Other MSA/CMSA	0	2	0	0	2	19						
Other Not MSA	0	14	0	1	9	43						

7.3.4 On-Road Concentrations Derived From Ambient Air Quality Adjusted to Just Meet the Current and Alternative Standards

Just as was done with the *as is* air quality data, on-road NO_2 concentrations were estimated using the air quality adjusted to just meeting the current and alternative standard and the approach described in section 7.2.3. The analysis was performed using the more recent air quality separated into two year-groups (2001-2003 and 2004-2006) based on the form of the potential alternative standards (i.e., a 3-year average). Results are presented in a manner consistent with section 7.3.3, whereby the number of exceedances of the potential benchmark levels were estimated. However, for the sake of brevity only key figures and tables are provided here. The complete results for the estimated on-road concentrations and numbers of benchmark exceedances are provided in Appendix A, section 9.

Figure 7-4 illustrates the estimated mean number of exceedances of the 100, 150, and 200 ppb levels on-roads, given 2001-2003 air quality adjusted to just meeting the current annual average standard. Most locations contained an average of hundreds to thousands of estimated exceedances of 100 ppb, much greater than those estimated using either the ambient monitors sited < 100 m or ≥ 100 m of a major road (Figure 7-1). The estimated number of exceedances of the 150 and 200 ppb levels were also higher on-roads, most locations were estimated to contain several hundred exceedances of 150 ppb and a few hundred exceedances of 200 ppb using air quality concentrations adjusted to just meeting the current standard.

The effect of the potential alternative standards on the estimated on-road NO_2 concentrations was also analyzed at each of the locations. Figure 7-5 illustrates each of the standard levels (50, 100, 150, and 200 ppb 1-hour) and the two forms (98^{th} and 99^{th} percentiles) investigated, again using Chicago as an example to describe observed trends. The trends observed in Figure 7-2 and described in section 7.3.3 are similar to that observed here, albeit with greater numbers of exceedances estimated on-roads compared with those estimated for monitors near-roads or sited at a distance from major roads. Estimated numbers of concentrations above 100 ppb are several hundred to a thousand considering a standard level of 100 ppb (either perecentile), however exceedances of 200 ppb are estimated to be under one hundred.

Similar numbers of exceedances on-roads were estimated at other locations using air quality adjusted to just meeting the potential alternative standards. Figure 7-6 illustrates the estimated number of exceedances of 200 ppb at four selected locations as an example, Phoenix, Los Angeles, Philadelphia, and St. Louis, using a 98th percentile form of a 1-hour standard. The number of concentrations above 200 ppb is similar at each of the locations (including Chicago), particularly when comparing the 100 ppb standard level, ranging from tens to just under 100. Table 7-16 presents a more comprehensive comparison at this particular standard level (98th percentile at 100 ppb) using 2001-2003 adjusted air quality at each of the locations. For most locations, the estimated mean number of exceedances of 200 ppb on-roads was 100 or less, with upper percentiles estimated to number about one to several hundreds of exceedances. The mean number of exceedances of 250 and 300 ppb were less, ranging from a few to tens of occurrences in a year.

Tables 7-17 and 7-18 summarizes the observed and estimated mean numbers of exceedances of 100 and 150 ppb on-roads, respectively, using all the recent air quality *as is* and that adjusted to just meeting the current standard and the potential alternative 98th percentile standards at each location. Trends for the as is air quality and that adjusted to just meeting the current followed similar trends to that observed for the monitors sited ≥ 100 m and < 100 m of a major road (see Tables 7-14 and 7-15, for the 2001-2003 air quality). The estimated number of exceedances on-roads using the as is data fell within the range of estimates provided by the alternative 1-hour 98th percentile standards of 50 and 100 ppb, while the estimated on-road exceedances of 150 ppb fell within the range of provided by the 100 and 150 ppb alternative standards.

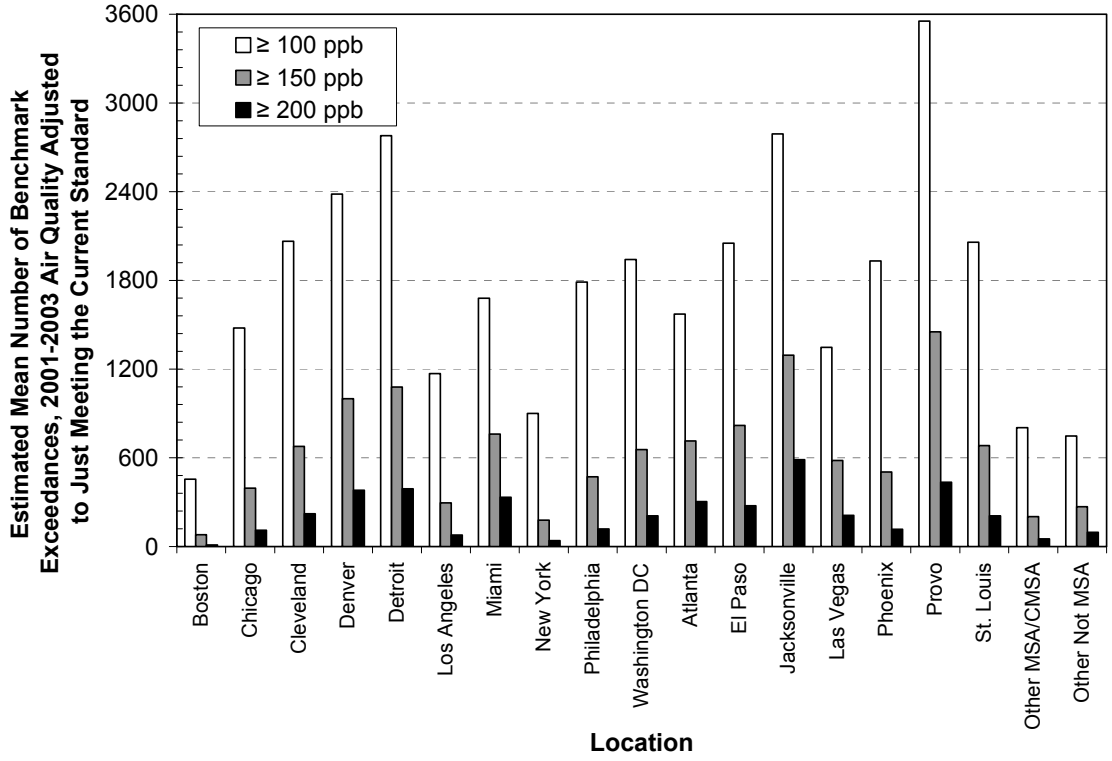


Figure 7-4. Estimated mean number of exceedances of selected 1-hour potential health effect benchmark levels on-roads, using 2001-2003 air quality adjusted to just meeting the current annual standard (0.053 ppm).

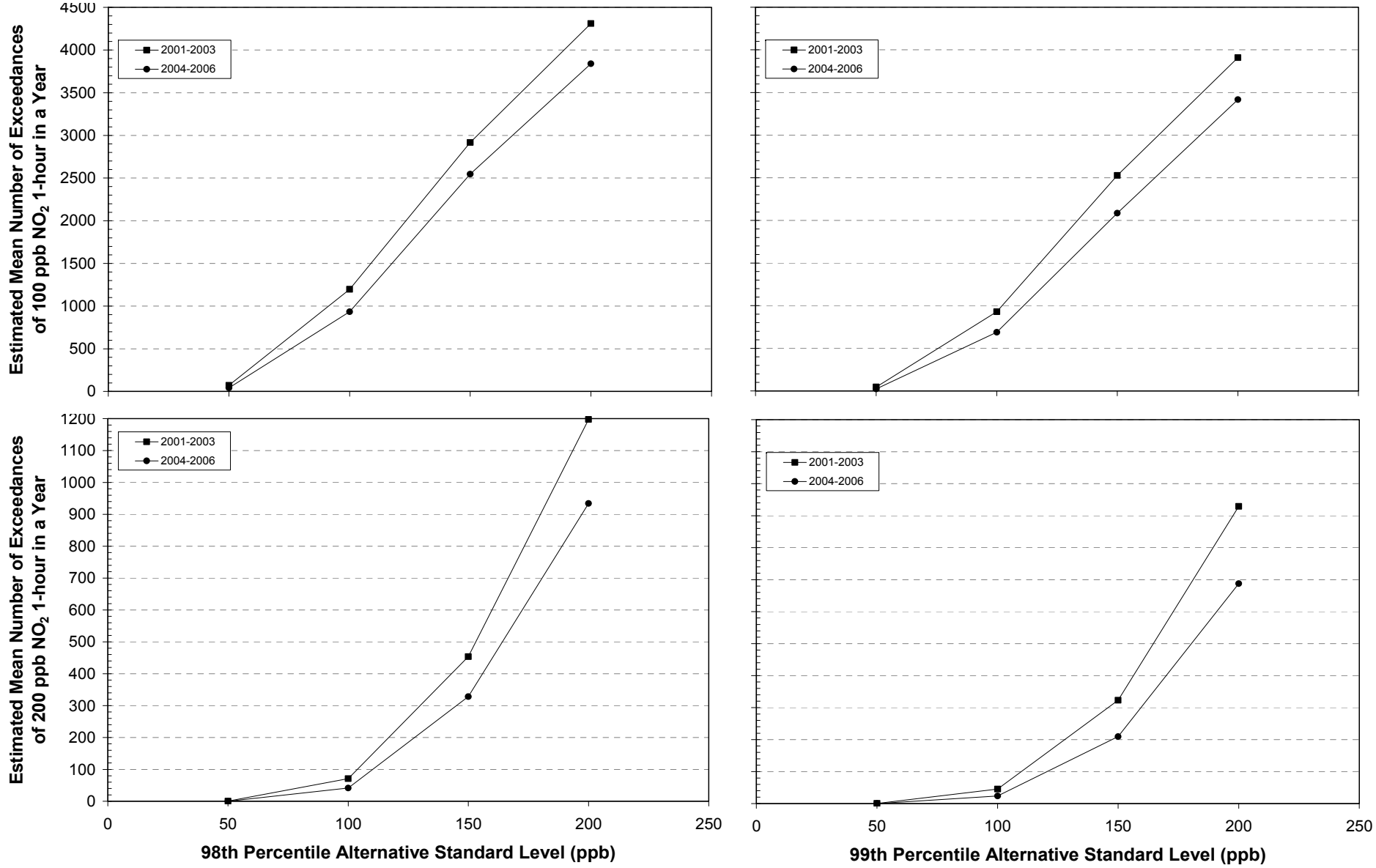


Figure 7-5. Estimated number of exceedances of potential health effect benchmarks (100 ppb, top; 200 ppb, bottom) on-roads in Chicago given just meeting alternative 1-hour standard levels (98th percentile, left; and 99th percentile, right) using recent air quality data.

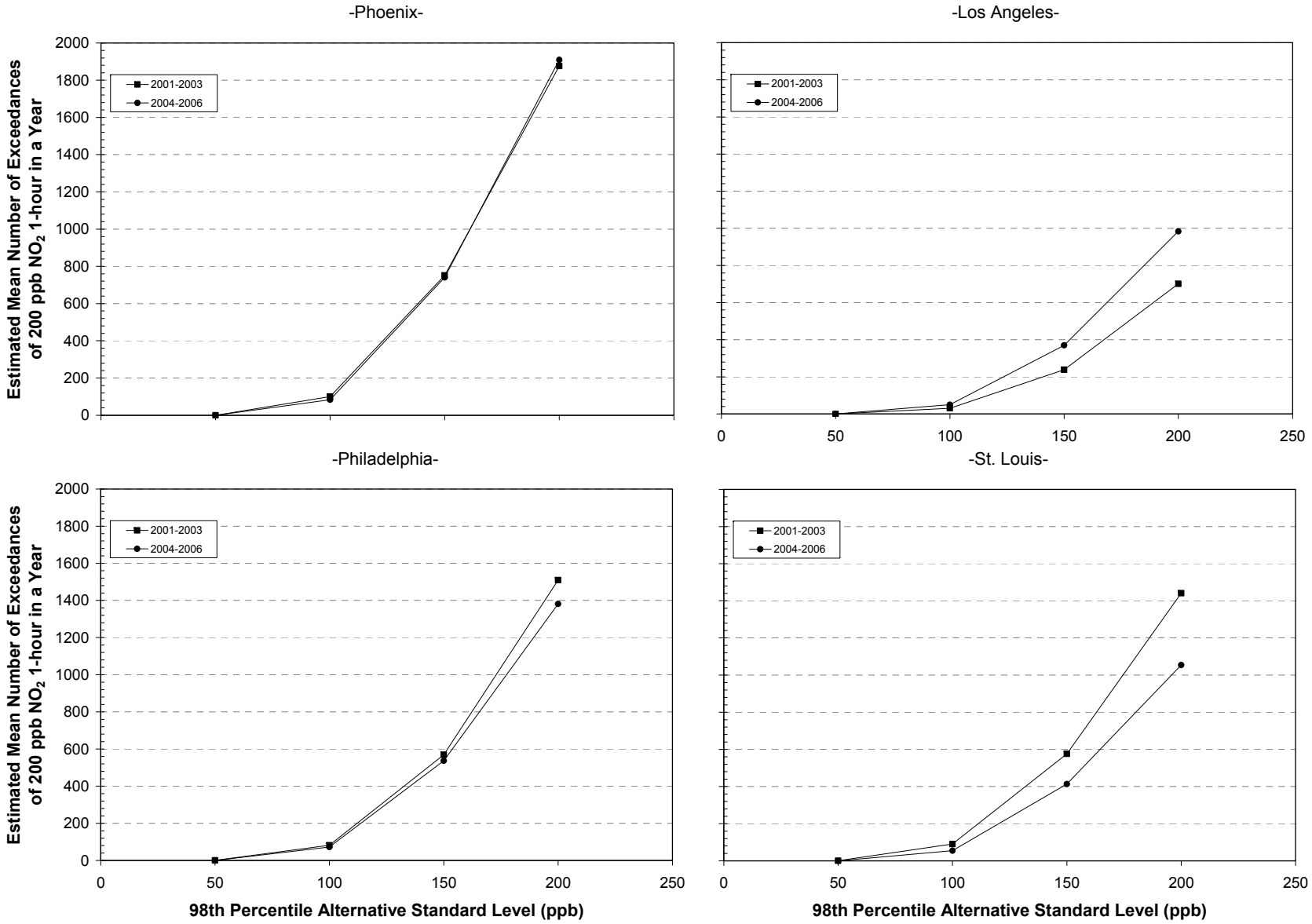


Figure 7-6. Estimated number of exceedances of 200 ppb in-roads in four locations (Phoenix, Los Angeles, Philadelphia, and St. Louis) given just meeting alternative 1-hour 98th percentile standard levels using recent air quality data.

Table 7-16. Estimated annual mean NO_2 concentration and the number of exceedances of 1-hour NO_2 concentration levels on-roads, using 2001-2003 air quality adjusted to just meeting a 1-hour 100 ppb 98th percentile alternative standard.

Location	Site-Years	Annual Mean NO_2 (ppb)				Number of Exceedances of 1-Hour Level																			
						≥ 100 ppb				≥ 150 ppb				≥ 200 ppb				≥ 250 ppb				≥ 300 ppb			
		Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99	Mean	Min	Med	p99
Boston	600	33	13	34	57	411	1	302	1511	66	0	12	541	8	0	0	90	1	0	0	21	0	0	0	9
Chicago	900	60	33	58	104	1197	44	951	4002	283	0	138	1564	71	0	14	641	21	0	1	291	7	0	0	118
Cleveland	300	63	43	62	88	1306	254	1224	2727	327	33	256	1003	92	0	44	393	30	0	7	176	12	0	1	85
Denver	200	63	40	60	96	1589	265	1395	3446	383	11	237	1621	92	0	19	608	23	0	3	217	6	0	1	54
Detroit	600	72	46	69	110	1793	419	1670	3929	516	37	377	1748	157	1	100	629	61	1	31	312	29	0	7	162
Los Angeles	5100	48	7	47	96	701	0	450	3357	142	0	43	1145	31	0	3	374	7	0	0	117	2	0	0	36
Miami	600	40	22	39	62	820	56	771	2054	251	1	164	1215	80	0	30	647	24	0	4	291	8	0	0	118
New York	2600	52	20	49	105	906	0	661	3630	171	0	65	1310	37	0	6	412	11	0	0	181	4	0	0	74
Philadelphia	1400	63	32	58	116	1509	52	1288	4554	343	0	171	2045	82	0	18	706	23	0	1	350	7	0	0	153
Washington DC	1800	62	20	63	117	1445	1	1305	4550	401	0	183	2317	107	0	20	828	32	0	1	297	10	0	0	135
Atlanta	1400	39	9	42	93	704	0	470	3040	191	0	44	1556	53	0	3	624	16	0	0	225	5	0	0	91
El Paso	1200	51	24	50	82	1097	62	988	2693	256	2	154	1302	57	0	21	403	15	0	4	107	4	0	0	34
Jacksonville	200	66	46	65	93	1374	451	1312	2842	422	25	370	1185	121	3	74	491	34	0	16	189	11	0	5	61
Las Vegas	1600	35	5	25	94	839	0	272	3736	232	0	37	2062	61	0	2	687	19	0	0	328	5	0	0	132
Phoenix	500	71	41	69	112	1876	77	1820	4400	462	2	278	2165	100	0	11	769	19	0	0	156	4	0	0	43
Provo	300	85	55	82	127	2950	664	2998	5067	913	19	715	3311	227	1	83	1512	60	0	4	401	19	0	0	178
St. Louis	900	63	36	61	99	1441	93	1321	3589	366	0	227	1766	91	0	26	663	25	0	3	243	8	0	0	113
Other MSA/CMSA	61200	30	1	29	65	188	0	52	1555	24	0	1	358	4	0	0	89	1	0	0	18	0	0	0	4
Other Not MSA	12700	24	3	21	67	202	0	33	1700	38	0	2	564	9	0	0	154	3	0	0	59	1	0	0	27

Table 7-17. Estimated mean number of exceedances of 100 ppb 1-hour NO_2 concentrations on-roads, using air quality as is and that adjusted to just meeting the current and alternative standards (98th percentile).

Location	2001-2003 Air Quality						2004-2006 Air Quality					
			Alternative 1-hour 98th percentile standard						Alternative 1-hour 98th percentile standard			
	As is	Current std	50	100	150	200	As is	Current std	50	100	150	200
Boston	12	455	8	411	1172	1865	5	462	8	372	1045	1735
Chicago	252	1478	71	1197	2918	4311	151	1357	42	934	2546	3841
Cleveland	103	2065	92	1306	2996	4402						
Denver	403	2384	92	1589	3064	3801	294	2163	181	1971	3235	3842
Detroit	185	2779	157	1793	3642	4863	81	2835	170	1834	3440	4552
Los Angeles	414	1170	31	701	2081	3258	177	1184	50	984	2390	3366
Miami	21	1680	80	820	1743	2504	17	1487	47	586	1284	1863
New York	205	900	37	906	2430	3598	168	1050	51	1072	2596	3774
Philadelphia	161	1788	82	1509	3340	4566	87	1914	72	1381	2992	4127
Washington DC	156	1941	107	1445	3041	4247	80	1697	75	1202	2575	3639
Atlanta	98	1572	53	704	1550	2296	59	1665	43	673	1487	2200
El Paso	85	2053	57	1097	2353	3215	67	2324	78	1200	2426	3214
Jacksonville	34	2790	121	1374	2916	4086	45	2755	131	1280	2673	3839
Las Vegas	88	1347	61	839	1605	2143	55	1206	61	767	1416	1932
Phoenix	527	1932	100	1876	3841	4880	353	2309	83	1909	3807	4812
Provo	241	3555	227	2950	4716	5567	394	2971	195	678	1995	3195
St. Louis	91	2057	91	1441	3129	4483	50	1785	55	1055	2434	3650
Other MSA/CMSA	54	804	4	188	760	1451	32	886	11	359	1101	1859
Other Not MSA	9	748	9	202	610	1078	10	737	9	197	590	1008

Table 7-18. Estimated mean number of exceedances of 150 ppb 1-hour NO_2 concentrations on-roads, using air quality as is and that adjusted to just meeting the current and alternative standards (98th percentile).

Location	2001-2003 Air Quality						2004-2006 Air Quality					
	As is	Current std	Alternative 1-hour 98th percentile standard				As is	Current std	Alternative 1-hour 98th percentile standard			
			50	100	150	200			50	100	150	200
Boston	0	79	0	66	411	922	0	91	0	64	372	819
Chicago	33	395	7	283	1197	2362	15	335	2	190	934	1996
Cleveland	14	677	12	327	1306	2440						
Denver	51	999	6	383	1589	2692	34	761	16	626	1971	2922
Detroit	34	1079	29	516	1793	3112	6	1263	16	581	1834	2966
Los Angeles	67	295	2	142	701	1607	18	296	3	220	984	1944
Miami	1	761	8	251	820	1457	1	745	4	170	586	1066
New York	24	178	4	171	906	1944	17	226	4	231	1072	2129
Philadelphia	17	472	7	343	1509	2790	5	623	4	325	1381	2504
Washington DC	17	656	10	401	1445	2574	5	587	5	316	1202	2150
Atlanta	12	714	5	191	704	1275	5	803	3	174	673	1221
El Paso	7	820	4	256	1097	1993	5	1114	6	317	1200	2069
Jacksonville	3	1295	11	422	1374	2412	11	1329	25	394	1280	2245
Las Vegas	10	583	5	232	839	1393	7	561	9	227	767	1225
Phoenix	57	503	4	462	1876	3300	25	640	3	436	1909	3305
Provo	21	1452	19	913	2950	4282	214	1360	71	266	678	1526
St. Louis	8	683	8	366	1441	2627	4	647	4	249	1055	1991
Other MSA/CMSA	5	203	0	24	188	540	2	265	1	63	359	839
Other Not MSA	1	269	1	38	202	470	1	274	1	41	197	439

7.4 UNCERTAINTY ANALYSIS

This uncertainty analysis first identifies the sources of the assessment that do or do not contribute to uncertainty, and provide a rationale for why this is the case. A qualitative evaluation follows for the types and components of uncertainty, resulting in a summary describing, for each source of uncertainty, the direction of influence the uncertainty may have on the surrogate exposure estimates. This bias direction indicates how the source of uncertainty is judged to influence estimated concentrations, either the concentrations are likely "over-" or "under-estimated". In the instance where two or more types or components of uncertainty result in offsetting direction of influence, the uncertainty was judged as "both". "Unknown" was assigned where there was no evidence reviewed to judge the uncertainty associated with the source. Table 7-19 provides a summary of the sources of uncertainty identified in the air quality characterization and the overall judged bias of each.

7.4.1 Air Quality Data

One basic assumption is that the AQS NO_2 air quality data used are quality assured already. Reported concentrations contain only valid measures, since values with quality limitations are either removed or flagged. There is likely no selective bias in retention of data that is not of reasonable quality, it is assumed that selection of high concentration poor quality data would be just as likely as low concentration data of poor quality. Given the numbers of measurements used for this analysis, it is likely that even if a few low quality data are present in the data set, they would not have any significant effect on the results presented here. Therefore, the air quality data and database used likely 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 the temporal and spatial variability are represented. In particular, missing hourly measurements at a monitor may introduce bias (if different periods within a year or different years have different numbers of measured values) and increase the uncertainty. Furthermore, the spatial representativeness will be poor if the monitoring network is not dense enough to resolve the spatial variability (causing

increased uncertainty) or if the monitors are not evenly distributed (causing a bias). Additional uncertainty regarding temporal and spatial representation by the monitors is expanded below.

7.4.2 Measurement Technique for Ambient NO_2

One source of uncertainty for NO_2 air quality data is 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 (ISA, section 2.5.3.3), thus monitors positioned on rooftops may underestimate exposures. Only 7 of the 177[12] monitors in the named locations contained monitoring heights of 15 meters or greater, with nearly 60% at 4 meters or less height, and 80% at 5 meters or less in height. Not accounting for this potential vertical gradient in NO_2 concentrations may generate underestimates of exceedances for some sites, however the overall impact of inferences made for the locations included in this assessment is likely minimal since most monitors are sited at less than 4-5 meters in vertical height. In addition, the relationship at heights below 4 meters is uncertain (e.g., a breathing height of 2 meters is commonly used) and therefore would add an unknown bias to the estimated NO_2 concentrations above a benchmark when used as a surrogate for human exposure.

7.4.3 Temporal Representation

Data are valid hourly measures and are of similar temporal scale as identified health effect benchmark concentrations. There are frequent missing values within a given valid year which contribute to the uncertainty as well as introducing a possible bias if some seasons, day types (e.g., weekday/weekend), or time of the day (e.g., night or day) are not equally represented. Since a 75 percent daily and hourly completeness rule was applied, some of these uncertainties and biases were reduced in these analyses. Data were not interpolated in the analysis. Similarly, there may be bias and uncertainty if the years monitored vary significantly between locations. Although monitoring locations within a region do change over time, the NO_2 network has been reasonably stable over the 1995-2006 period, particularly at locations with larger monitoring networks, so the impact to uncertainty is expected to be minimal regarding the bias direction. It

[12] 28 monitors did not have height reported (therefore, 177 + 28 = 205 total number of monitors in named locations)

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 is not the case. Separating the data into two 6-year groups (historic and recent for the as is evaluation) and two further subsets of the more recent air quality (2001-2003 and 2004-2006) before analysis reduces the potential impact from changes in national- or location-specific source influences and is judged to have a minimal bias.

7.4.4 Spatial Representation

Relative to the physical area, there are only a small number of monitors in each location. Since most locations have sparse siting, the monitoring data are assumed to be spatially representative of the locations analyzed here. This includes areas between the ambient monitors that may or may not be influenced by similar local sources of NO_2. For these reasons the uncertainty and bias due to the spatial network may be moderate, although the monitoring network design should have addressed these issues within the available resources and other monitoring constraints. Bias would be most prevalent in locations with the fewest monitors, although the direction being largely unknown. In addition, the air quality characterization used all monitors meeting the 75 percent completeness criteria, without taking into account the monitoring objectives or land use for the monitors. Thus, there will be some lack of spatial representation and uncertainty due to the inclusion/exclusion of some monitors that are very near local sources (including mobile sources) resulting in both over- or under- estimations.

7.4.5 Air Quality Adjustment Procedure

There is uncertainty in the air quality adjustment procedures due to the uncertainty of the true relationship between the adjusted concentrations and the as is air quality. The adjustment factors used for the current and alternative standards each assumed that all hourly concentrations will change proportionately. However, the impact of the adjustment on the estimated concentrations is a function of the particular form and level of the standard simulated and, depending on whether concentrations are adjusted upwards or downward, will vary.

Different sources have different temporal emission profiles, so that equally applied changes to the concentrations at the ambient monitors to simulate hypothetical changes in emissions may not correspond well with all portions of the concentration distribution. When adjusting concentrations upward to just meeting the current standard, the proportional adjustment

used an equivalent multiplicative factor for all portions of the concentration distribution, the upper tails were treated the same as the area of central tendency. This may not necessarily reflect changes in an overall emissions profile that may result from, for example, an increase in the number of sources in a location. It is possible that while the mean concentration measured at an ambient monitor may increase with an increase in the sources affecting concentrations measured at the monitor, the tails of the distribution might not have a proportional increase. Adjusting the ambient concentrations upwards to simulate the alternative standards also carries a similar degree of uncertainty however the multiplicative factors are derived from the upper percentiles of the 1-hour concentrations and applied to the 1-hour concentrations equally. In each of these instances of adjusting the concentrations upwards, there may be an associated over-estimation in the concentrations at the upper tails of the distributions, leading to over-estimation in the numbers of exceedances. In adjusting concentrations downward (e.g., the alternative standard level of 50 ppb 1-hour, 99th percentile), the use of a proportional multiplicative adjustment derived from and applied to the upper tails of the concentration distribution may better represent what might occur to emissions with added source controls. However it is likely that the mean concentrations and lower percentiles of the distribution are under-estimated.

Similarly, emission changes that would affect the concentrations at the design monitor containing the highest concentration (annual mean, 98th or 99th percentile 1-hour) may not necessarily impact lower concentration sites proportionately. This could result in overestimations in the number of exceedances at lower concentration sites within a location, however it is likely to be minimal given that the greatest numbers of exceedances typically were measured at the monitoring sites with the highest concentrations within the location (Appendix A, section 7). This bias would be less in locations containing several monitors, such as Boston, New York, or Los Angeles. Universal application of the proportional simulation approach at each of the locations was done for consistency and was designed to preserve the inherent variability in the concentration profile. A few locations were noted that may have an exceptional number of estimated exceedances as a result of the air quality adjustment approach, particularly those locations with few monitoring sites that contained very low concentrations and/or atypical variability in hourly concentrations. These few locations (e.g., Miami, Jacksonville, Provo) may contain overestimations at the upper tails of the concentration distribution, leading to bias in

estimated number of exceedances at both the upper percentiles and the mean when using the air quality simulated to just meet the current standards.

7.4.6 On-Road Concentration Simulation

On-road and ambient monitoring NO_2 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 in this analysis to estimate on-road NO_2 concentrations was derived from data collected in measurement studies containing 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 in this analysis to estimate on-road hourly concentrations from hourly ambient measures, assuming a direct relationship exists between the short-term peaks to time-averaged concentrations (e.g., hourly on-road 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. The on-road concentration estimation also assumes that concentration changes that occur on-road and at the monitor are simultaneous (i.e., within the hour time period of estimation). Since time-activity patterns of individuals are not considered in this analysis, there is no bias in the number of estimated exceedances. The long-term data used to develop the algorithm used 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. This could result in either over- or under-estimations of concentrations, depending on the time of day. The variability in NO_2 concentration within an hour was also not considered in this analysis, that is, the on-road concentration at a given site will likely vary during the 1-hour time period. If considering personal exposures to individuals within vehicles that are traveling on a road, it is likely that their exposure concentrations would also vary due to differing roadway concentrations. This could also result in either over- or under-estimations of concentrations, depending on the duration of travel and type of road traveled on.

On-road concentrations were not modified in this analysis to account for in-vehicle penetration and decay. Therefore, in-vehicle concentrations would be overestimated if using the on-road concentrations as a surrogate, given that reactive pollutants (e.g., $PM_{2.5}$) tend to have a lower indoor/outdoor (I/O) concentration ratio (Rodes et al., 1998). Chan and Chung (2003) report mean (I/O) ratios of NO_2 for a few roadways and driving conditions in Hong Kong. On highways and urban streets, the value is centered about 0.6 to 1.0, indicating decay of NO_2 as it enters the vehicle.

At locations where traffic counts are very low (e.g., on the order of hundreds/day) the on-road contribution has been shown to be negligible (Bell and Ashenden, 1997; Cape et al., 2004), therefore any monitors sited in rural areas with minimal traffic volumes may result in small overestimations of NO_2 concentrations using equation (7-2) at these locations. Monitors sited within 100 m of the roadway were not used in the calculation of on-road concentrations due to the possibility of these monitors already accounting for notable impact from vehicle emissions (e.g., Beckerman et al., 2008), thus controlling for a double-counting of on-road concentrations. However, there is potential for influence by non-road source emissions on the measured concentrations at the monitors used ($\geq$ 100 m froma major road), contrary to an assumption that there is an absence of direct source influence (only mobile sources were controlled for by selecting monitors these monitors). Therefore, at certain monitors directly affected by emissions from non-road sources, the simulated on-road concentrations may be over-estimated. Another source of uncertainty in the spatial heterogeneity of NO_2 concentrations regards the presence of street canyons on roadways. These localized areas may be subject to highly variable concentrations within a short span of a road, often defined by the presence of man-made structures, such as buildings, on both sides of the road. A comparison of street canyon measured NO_x concentrations with those measured at a reference site (termed background) indicate that there is about a factor of 2.3 difference in the concentrations (Ghenu et. al, 2007). Vardoulakis et al. (2004) reported mean NO_2 concentrations at a major intersection can be a factor of about 2.1 times greater than on-road concentrations measured at a few hundred meters distance within a street canyon.[13] Because these factors are within the range of simulation factors used here in estimating the on-road concentration, i.e., ranging from a factor of 1.2 to 3.7 times the ambient

[13] Ambient concentrations at a site not influenced by mobile sources were not reported in this Vardoulakis et al. (2004).

concentrations, it is likely that some of the estimated on-road concentrations are similar in magnitude to those found in street canyons. In addition, NO_x is primarily emitted as NO (e.g., Heeb et al., 2008; Shorter et al., 2005), with substantial secondary formation due predominantly to $NO + O_3 \rightarrow NO_2 + O_2$. Numerous studies have demonstrated the O_3 reduction that occurs near major roads, reflecting the transfer of odd oxygen to NO to form NO_2, a process that can impact NO_2 concentrations both on- and downwind of the road. Some studies report NO_2 concentrations increasing just downwind of roadways and that are inversely correlated with O_3 (e.g., Beckerman et al., 2008), suggesting that peak concentration of NO_2 may not always occur on the road, but at a distance downwind. Uncertainty regarding where the peak concentration occurs (on-road or at a distance from the road) in combination with the form of the exponential model used to estimate the on-road concentrations (the highest concentration occurs at zero distance from road) may also lead to overestimation in the number of exceedances.

Another source of uncertainty is the extent to which the near-road study locations used to derive the on-road simulation factors represent the locations in these analyses. The on-road and near-road data were collected in a few locations, most of them outside of the United States. The source mixes (i.e., the vehicle fleet) in study locations may not be representative of the U.S. fleet. Without detailed information characterizing the emissions patterns for the on-road study areas, there was no attempt to match the air quality characterization locations to specific on-road study areas, which might have improved the precision of the estimates. However, since concentration ratios were selected randomly from all the near-road studies and applied to each monitor individually, and since we estimated overall minimum and upper bounds using multiple simulations, the analysis provides a reasonable lower and upper bound estimates of the number of exceedances.

7.4.7 Health Benchmark

The choice of potential health effect benchmarks, and the use of those benchmarks to assess risks, can introduce uncertainty into the risk assessment. For example, the potential health effect benchmarks used were based on studies where volunteers were exposed to NO_2 for varying lengths of time. Typically, the NO_2 exposure durations were between 30 minutes and 2 hours. This introduces some uncertainty into the characterization of risk, which compared the potential health effect benchmarks to estimates of exposure over a 1-hour time period. Use of a

1-hour averaging time could over- or under-estimate risks. In addition, the human exposure studies evaluated airways responsiveness in mild asthmatics. For ethical reasons, more severely affected asthmatics and asthmatic children were not included in these studies. Severe asthmatics and/or asthmatic children may be more susceptible than mildly asthmatic adults to the effects of NO_2 exposure. Therefore, the potential health effect benchmarks based on these studies could underestimate risks in populations with greater susceptibility.

Table 7-19. Summary of qualitative uncertainty analysis for the air quality and health risk characterization.

Source	Type	Bias Direction
Air Quality Data	Database quality	both
Ambient Measurement	Interference	over
	Vertical siting	under
	No Extrapolation < 4m	unknown
Temporal Representation	Scale	none
	Missing data	both
	Years monitored	both
	Source changes	over
Spatial Representation	Scale	unknown
	Monitor objectives	both
Air Quality Adjustment	Temporal scale	over
	Spatial scale	over
On-Road Simulation	Temporal scale	both
	Decay	over
	Spatial scale	over
	Model used	over
	Non US studies used	unknown
Health Benchmarks	Averaging time	unknown
	Susceptibility	under
Notes: Bias Direction: indicates the direction the source of uncertainty is judged to influence either the concentration or risk estimates		

8. EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION

9. CHARACTERIZATION OF HEALTH RISKS USING DATA FROM EPIDEMIOLOGICAL STUDIES

9.1 INTRODUCTION

As mentioned above in chapter 6, in response to advice received from the CASAC NO_2 Panel on the 1st draft REA, we have conducted a focused quantitative risk assessment in which estimates of respiratory ED visits as a function of ambient levels of NO_2 have been developed for a single urban area (i.e., the Atlanta MSA). In this approach, concentration-response functions are derived from NO_2 epidemiological studies and are used in conjunction with ambient air quality data representing alternative air quality scenarios and baseline incidence data to estimate the impact of ambient levels of NO_2 on ED visits associated with these air quality scenarios. The purpose for the current risk assessment is to present an illustrative case study that provides information on the magnitude and potential changes in NO_2-related public health impacts associated with recent air quality and alternative air quality scenarios simulating attainment of the current and alternative NO_2 standards. Chapters 4 and 5 of this document provide additional qualitative assessment of the epidemiological evidence most relevant to characterizing NO_2-related health effects in the United States including respiratory-related ED visits as well as other health endpoints. As described in chapter 1, the Agency's views on policy options addressing the adequacy of the current standard and alternative standards that takes into consideration both the final results of the risk assessment discussed in this chapter, as well as the air quality and exposure assessments presented in chapters 7 and 8, and the scientific evidence evaluated in the ISA will be presented in the next step of the NAAQS-review process in an ANPR published in the Federal Register.

Previous reviews of the NO_2 primary NAAQS, completed in 1985 and 1996, did not include quantitative health risk assessments. Thus, the risk assessment described in this document builds upon the methodology and lessons learned from the risk assessment work conducted for the recently concluded PM and O_3 NAAQS reviews (Abt Associates, 2005; Abt Associates, 2007). Many of the same methodological issues are present in conducting a risk assessment for each of these criteria air pollutants where epidemiological studies provided the basis for the concentration-response relationships used in the quantitative risk assessment.

The NO_2 health risk assessment described in this chapter estimates the incidence of respiratory-related ED visits associated with short-term exposures to NO_2 under recent ("as is") air quality levels, upon just meeting the current NO_2 standard of 0.053 ppm annual average, and upon just meeting several potential alternative NO_2 primary NAAQS in the Atlanta MSA.[14] As discussed in more detail in chapter 6 above, staff has elected to evaluate daily maximum 1-h standard levels of 0.05, 0.10, 0.15, and 0.20 ppm using both 98th and 99th percentile forms and averaged over a thee-year period.[15] The risk assessment is intended as a tool that, together with other information on this health endpoint and other health effects evaluated in the final ISA and discussed elsewhere in this document, can aid the Administrator in judging whether the current primary standard protects public health with an adequate margin of safety, or whether revisions to the standard are appropriate.

Section 9.2 describes the general approach used to conduct the risk assessment for ED visits. Sections 9.3, 9.4, and 9.5 discuss in more detail the three types of inputs required to conduct the assessment. Section 9.6 presents a discussion of uncertainties and variability and section 9.7 presents a summary of results from the assessment and key observations.

9.2 GENERAL APPROACH

The general approach used for the NO_2-related ED risk assessment is dictated by the fact that it is based on concentration-response functions which have been estimated in epidemiological studies evaluated in the final ISA. Since these studies estimate concentration-response functions using ambient air quality data from fixed-site, population-oriented monitors, the appropriate application of these functions in a risk assessment similarly requires the use of ambient air quality data at fixed-site, population-oriented monitors. In order to estimate the incidence of respiratory-related ED visits associated with recent air quality conditions in a set of counties attributable to ambient NO_2 exposures, as well as the change in incidence of this health effect in that set of counties corresponding to a given simulated change in NO_2 levels representing just meeting the current or alternative 1-h daily maximum NO_2 standards, the following thee elements are required:

[14] The current NO_2 standard refers to a two-year period and requires that the annual average NO_2 level be less than or equal to 0.053 ppm in each of the two years.

[15] As an example, for the alternative standards using the 98th percentile form, the standard is met when the average of the annual 98th percentile daily maximum 1-hour concentrations for a 3-year period is at or below the specified standard level.

- **Air quality information** including: (1) "as is" air quality data for NO_2 from ambient monitors in the assessment location, and (2) "as is" concentrations adjusted to reflect patterns of air quality estimated to occur under a simulation where the area's air quality is adjusted to just meet the specified standard. (These air quality inputs are discussed in more detail in section 6.2 of this document).

- **Concentration-response functions** which provide an estimate of the relationship between the health endpoint of interest and ambient NO_2 concentrations.

- **Baseline health effects incidence.** The baseline incidence of the health effect in the assessment location in the target year is the incidence corresponding to "as is" NO_2 levels in that location in that year.

Figure 9-1 provides a broad schematic depicting the role of these components in the NO_2 risk assessment. Each of the key components (i.e., air quality information, estimated concentration-response functions, and baseline incidence) is discussed below, highlighting those points at which judgments have been made.

These inputs are combined to estimate health effect incidence changes associated with specified changes in NO_2 levels. Although some epidemiological studies have estimated linear or logistic concentration-response functions, by far the most common form, and the form relevant for the epidemiological study used in the current risk assessment is the exponential (or log-linear) form:

$$y = Be^{\beta x}, \qquad \text{(Equation 9-1)}$$

where x is the ambient NO_2 level, y is the incidence of the health endpoint of interest at NO_2 level x, β is the coefficient of ambient NO_2 concentration (describing the extent of change in y with a unit change in x), and B is the incidence at x=0, i.e., when there is no ambient NO_2. The relationship between a specified ambient NO_2 level, x_0, for example, and the incidence of a given health endpoint associated with that level (denoted as y_0) is then

$$y_0 = Be^{\beta x_0}. \qquad \text{(Equation 9-2)}$$

If we let x_0 denote the baseline (upper) NO_2 level, and x_1 denote the lower NO_2 level, and y_0 and y_1 denote the corresponding incidences of the health effect, we can derive the following

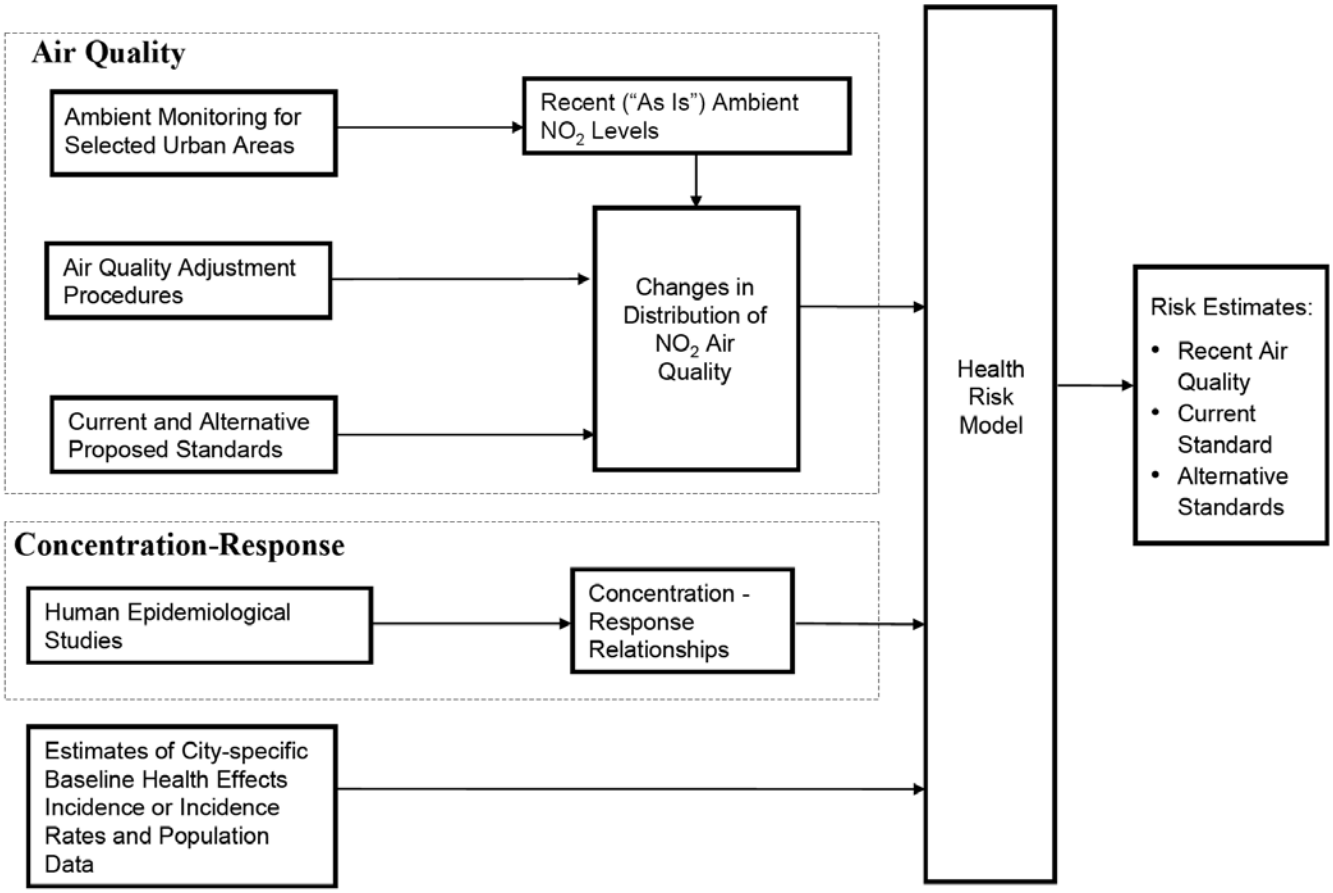


Figure 9-1. Major components of nitrogen dioxide health risk assessment for emergency department visits.

relationship between the change in x, $\Delta x = (x_0 - x_1)$, and the corresponding change in y, Δy, from equation (9-1)[16]:

$$\Delta y = (y_0 - y_1) = y_0[1 - e^{-\beta \Delta x}]. \quad \text{(Equation 9-3)}$$

Alternatively, the difference in health effects incidence can be calculated indirectly using relative risk. Relative risk (RR) is a measure commonly used by epidemiologists to characterize the comparative health effects associated with a particular air quality comparison. The risk of ED visits for respiratory illness at ambient NO_2 level x_0 relative to the risk of ED visits for respiratory illness at ambient NO_2 level x_1, for example, may be characterized by the ratio of the two rates: the rate of ED visits for respiratory illness among individuals when the ambient NO_2 level is x_0 and the rate of ED visits for respiratory illness among (otherwise identical) individuals when the ambient NO_2 level is x_1. This is the RR for ED visits for respiratory illness associated with the difference between the two ambient NO_2 levels, x_0 and x_1. Given a concentration-response function of the form shown in equation (9-1) and a particular difference in ambient NO_2 levels, Δx, the RR associated with that difference in ambient NO_2, denoted as $RR_{\Delta x}$, is equal to $e^{\beta \Delta x}$. The difference in health effects incidence, Δy, corresponding to a given difference in ambient NO_2 levels, Δx, can then be calculated based on this $RR_{\Delta x}$ as

$$\Delta y = (y_0 - y_1) = y_0[1 - (1/RR_{\Delta x})]. \quad \text{(Equation 9-4)}$$

Equations (9-3) and (9-4) are simply alternative ways of expressing the relationship between a given difference in ambient NO_2 levels, $\Delta x > 0$, and the corresponding difference in health effects incidence, Δy. These health impact equations are the key equations that combine air quality information, concentration-response function information, and baseline health effects incidence information to estimate health risks related to changes in ambient NO_2 concentrations.

[16] If $\Delta x < 0$ – i.e., if $\Delta x = (x_1 - x_0)$ – then the relationship between Δx and Δy can be shown to be $\Delta y = (y_1 - y_0) = y_0[e^{\beta \Delta x} - 1]$. If $\Delta x < 0$, Δy will similarly be negative. However, the *magnitude* of Δy will be the same whether $\Delta x > 0$ or $\Delta x < 0$ – i.e., the absolute value of Δy does not depend on which equation is used.

9.3 AIR QUALITY INFORMATION

As illustrated in Figure 9-1, and noted earlier, air quality information required to conduct the NO_2 risk assessment includes (1) recent air quality data for NO_2 from a suitable monitor for the assessment location and (2) air quality adjustment procedures to modify the recent data to simulate air quality data just meeting the current annual and potential alternative 1-h daily maximum standards. The approach used to adjust air quality data to simulate meeting specified standards is discussed above in section 6.2.

In the first part of the risk assessment, we estimate the incidence of the health effect associated with "as is" levels of NO_2 (or equivalently, the change in health effect incidence, Δy, associated with a change in NO_2 concentrations from "as is" levels of NO_2 to 0 ppb). In the second part, we estimate the incidence of the health effect associated with NO_2 concentrations simulated to just meet a specified standard (i.e., the current NO_2 standard of 0.053 ppm annual average as well as each of potential alternative 1-h daily maximum standards).

To estimate the incidence of a health effect associated with "as is" NO_2 levels in a location, we need a time series of hourly "as is" NO_2 concentrations for that location. We have used monitor data from the Georgia Tech monitor (monitor id =131210048), the monitor that was used in Tolbert et al. (2007), the epidemiological study from which we obtained the concentration-response functions (see section 9.4 below). Complete hourly data were available on over 93 percent of the days – 348 days in 2005, 345 days in 2006, and 340 days in 2007. Missing NO_2 concentrations were filled in, as described in section 3.5 of Appendix C.

Because Tolbert et al. (2007) estimated a relationship between daily respiratory-related ED visits and the 3-day moving average (i.e., NO_2 levels on the same day, the previous day, and the day before that) of the daily 1-h maximum NO_2 concentrations, we calculated the 3-day moving average of the daily 1-h maximum NO_2 concentrations at the monitor to provide the air quality input to the risk assessment.

The calculations for the second part of the risk assessment, in which we estimated risks associated with NO_2 levels simulated to just meet the current annual standard and potential alternative 1-h daily maximum standards were done analogously, using the monitor-specific series of adjusted daily maximum hourly concentrations rather than the monitor-specific series of "as is" daily maximum hourly concentrations.

9.4 CONCENTRATION-RESPONSE FUNCTIONS

As indicated in Figure 9-1, another key component in the risk assessment model is the set of concentration-response functions which provide estimates of the relationship between the health endpoint of interest and ambient NO_2 concentrations. As discussed above, the health endpoint of interest for this focused quantitative risk assessment is respiratory-related ED visits. As discussed in sections 4.2.2 and 4.5.2 several community epidemiological studies have been conducted in the U.S. that examined the relationship between NO_2 and other air pollutants and increased ED visits either for all respiratory causes or for asthma-related visits. Figure 5-1 in this document summarizes the single pollutant model effect estimates from these studies. As discussed in section 4.5.2, staff has considered several factors in selecting the urban area and epidemiological studies upon which the current risk assessment is based. First, we have judged that studies conducted in the United States are preferable to those conducted outside the United States given the potential for effect estimates to be impacted by factors such as the ambient pollutant mix, the placement of monitors, activity patterns of the population, and characteristics of the healthcare system. Second, we judged that studies of ambient NO_2 are preferable to those of indoor NO_2 given that studies of indoor NO_2 focus on exposures in locations with indoor sources of NO_2. These indoor sources can result in exposure patterns, NO_2 levels, and co-pollutants that are different from those typically associated with ambient NO_2. Third, we judged it appropriate to focus on studies of ED visits. When compared to studies of respiratory symptoms, the public health significance of ED visits is less ambiguous for the individuals affected. In addition, baseline incidence data are more readily available for these endpoints. Finally, we judged it appropriate to focus on studies that evaluated NO_2 health effect associations using both single- and multi-pollutant models. Taking these factors into consideration, we have chosen to focus on the studies by Tolbert and colleagues (2007) in Atlanta, Georgia that address ED visits for respiratory causes as a case study to illustrate the magnitude and changes in estimated NO_2-related risks for this endpoint for various air quality scenarios.

Tolbert et al. (2007) estimated concentration-response functions using both single pollutant models (i.e., where NO_2 was the only pollutant entered into the health effects model) and multi-pollutant models (i.e., where one or two co-pollutants (PM_{10}, O_3, CO) were entered into the health effects model). 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 concentration-response functions are based on single pollutant models. However, if co-pollutants are highly correlated with NO_2, their inclusion in an NO_2 health effects model can lead to misleading conclusions in identifying a specific causal pollutant. When collinearity exists, inclusion of multiple pollutants in models often produces unstable and statistically insignificant effect estimates for both 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, we report risk estimates based on both single- and multi-pollutant models in the NO_2 risk assessment.

All of the models in Tolbert et al. (2007) used a 3-day moving average of pollution levels (i.e., the average of 0-, 1-, and 2-day lags), so the issue of which of several different lag structures to select does not arise. The issue of how well a given lag structure captures the actual relationship between the pollutant and the health effect, however, is still relevant. Models in which the pollutant-related incidence on a given day depends only on same-day or previous-day pollutant concentration (or some variant of those, such as a two- or thee-day average concentration) necessarily assume that the longer pattern of pollutant levels preceding the pollutant concentration on a given day does not affect incidence of the health effect on that day. To the extent that a pollutant-related health effect on a given day is affected by pollutant concentrations over a longer period of time, then these models would be mis-specified, and this mis-specification would affect the predictions of daily incidence based on the model. The extent to which short-term NO_2 exposure studies may not capture the possible impact of long-term exposures to NO_2 is unknown. A number of epidemiologic studies have examined the effects of long-term exposure to NO_2 and observed associations with decrements in lung function and partially irreversible decrements in lung function growth. The final ISA (EPA, 2008a) concludes, however, that "overall, the epidemiological evidence was suggestive but not sufficient to infer a causal relationship between long-term NO_2 exposure and respiratory morbidity" (ISA, section 3.4). Currently, there is insufficient information to adequately adjust for the potential impact of longer-term exposure on respiratory ED visits associated with NO_2 exposures, if any, and this uncertainty should be kept in mind as one considers the results from the short-term exposure NO_2 risk assessment.

9.5 BASELINE HEALTH EFFECTS INCIDENCE DATA

As illustrated in Equation 9-1, the most common health risk model based on air pollution epidemiological studies expresses the reduction in health risk (Δy) associated with a given reduction in NO_2 concentrations (Δx) as a percentage of the baseline incidence (y). To accurately assess the impact of changes in NO_2 air quality on health risk in a given urban area, information on the baseline incidence of health effects in that location is therefore needed. For this assessment, baseline incidence is the incidence under recent ("as is") air quality conditions.

We obtained annual estimates of the baseline incidence of respiratory ED visits in Atlanta, GA via personal communication with the authors of the study conducted in the Atlanta area (Tolbert, 2007). Tolbert et al. (2007) notes that there are 42 hospitals with emergency departments in the 20-county Atlanta MSA. Of these, 41 were able to provide incidence data for at least part of the study period (1993 – 2004). For purposes of the NO_2 risk assessment, we need incidences for the years of the risk assessment (2005 – 2007). Assuming that baseline incidence of respiratory ED visits does not change appreciably in the span of a few years, we have used the incidence of respiratory ED visits for the most recent year (i.e., 2004) in the Tolbert et al. study, which was 121,818 respiratory ED visits.[17] Because this baseline incidence estimate is based on 36 hospitals, rather than the total 42 hospitals in Atlanta, this will be an underestimate of baseline incidence. This is a source of downward bias in our estimates of NO_2-related risk.

Average daily baseline incidences, necessary for short-term daily concentration-response functions, were calculated by dividing the annual incidence by the number of days in the year for which the baseline incidences were obtained. To the extent that NO_2 affects health, however, actual incidence rates would be expected to be somewhat higher than average on days with high NO_2 concentrations; using an average daily incidence would therefore result in underestimating the changes in incidence on such days. Similarly, actual incidence rates would be expected to be somewhat lower than average on days with low NO_2 concentrations; using an average daily incidence would, therefore, result in overestimating the changes in incidence on low NO_2 days. Both effects would be expected to be small, however, and should largely cancel one another out.

[17] The specific definition of "respiratory-related" emergency department visits used in Tolbert et al. (2007) included visits with the following respiratory illnesses as the primary diagnosis (specified by ICD-9 diagnostic codes): asthma (493, 786.07, and 786.09), COPD (491, 492, and 496), upper respiratory illness (460 – 465, 460.0, and 477), pneumonia (480 – 486), and bronchiolitis (466.1, 466.11, and 466.19).

9.6 ADDRESSING UNCERTAINTY AND VARIABILITY

An important issue associated with any population health risk assessment is the characterization of uncertainties and variability. *Uncertainty* refers to the lack of knowledge regarding both the actual values of model input variables (parameter uncertainty) and the physical systems or relationships (model uncertainty – e.g., the shape of the concentration-response functions). In any risk assessment, uncertainty is, ideally, reduced to the maximum extent possible, but significant uncertainty often remains. It can be reduced by improved measurement and improved model formulation. In addition, the degree of uncertainty can be characterized, sometimes quantitatively. For example, for the NO_2 risk assessment the statistical uncertainty surrounding the estimated NO_2 coefficients in the concentration-response functions is reflected in the confidence intervals provided for the risk estimates presented in this chapter and in Appendix C. Additional uncertainties are discussed briefly below and in more detail in Appendix C.

Variability refers to the heterogeneity in a population or variable of interest that is inherent and cannot be reduced though further research. The current risk assessment for Atlanta is based on locations-specific inputs (i.e., air quality data, baseline incidence data, and concentration-response functions are for the Atlanta MSA). Variability in air quality data is considered to some extent by the inclusion of thee years of data. Temporal variability is more difficult to address, because the risk assessment focuses on some unspecified time in the future when a given standard is just being met. To minimize the degree to which values of inputs to the analysis may be different from the values of those inputs at that unspecified time: we have used recent input data – for example, air quality data for the period 2005-2007 and baseline incidence data for 2004. However, future changes in these inputs have not been predicted (e.g., future population levels or changes in baseline incidence).

A number of important sources of uncertainty have been addressed qualitatively. Section 3.8 in Appendix C discusses in greater detail the uncertainties and variability present in the health risk assessment. The following is a brief discussion of the major sources of uncertainty and variability in the risk assessment and how they are dealt with or considered in the risk assessment:

- Causality. There is uncertainty about whether the association between NO_2 and ED visits actually reflects a causal relationship. Our judgment, drawing on the

conclusions in the ISA and as discussed in more detail in chapter 4, is that there is, at a minimum, a likely causal relationship with either short-term NO_2 itself or with NO_2 serving as an indicator for itself and other components of ambient air associated with combustion processes.

- Empirically estimated concentration-response relationships. In estimating the concentration-response relationships, there are uncertainties: (1) surrounding estimates of NO_2 coefficients in concentration-response functions used in the assessment, (2) concerning the specification of the concentration-response model (including the shape of the relationships) and whether or not a population threshold or non-linear relationship exists within the range of concentrations examined in the studies, and (3) concerning the possible role of co-pollutants. The uncertainty resulting from the statistical uncertainty associated with the estimated NO_2 coefficient in the concentration-response function has been characterized by confidence intervals reflecting sample size. These confidence intervals do not reflect the uncertainties related to the concentration-response functions, such as whether or not the model used in the epidemiological study is the correct model form. With respect to uncertainties about model form and whether or not a population threshold exists, the available epidemiological studies neither support nor refute the existence of thresholds at the population level. Concerning the possible role of co-pollutants in the Tolbert et al. (2007) study, NO2 was only moderately correlated with the other pollutants considered (i.e., PM_{10}, O_3) that produced the concentration-response functions that have been used in the risk assessment, although it was fairly highly correlated ($r = 0.7$) with CO. When a study, such as Tolbert et al. (2007) is conducted in a single location, the problem of possible confounding is particularly difficult. Single-pollutant models, which omit co-pollutants, may produce overestimates of the NO_2 effect, if some of the effects are really due to one or more of the other pollutants. On the other hand, effect estimates based on a multi-pollutant model can be uncertain and even result in statistically insignificant estimates where there is a true relationship, if the co-pollutants included in the model are highly correlated with NO_2. As a result of these considerations, we report risk estimates based on both the single- and multi-pollutant models from Tolbert et al. (2007). It should be noted that use of a concentration-response relationship based on an epidemiological study conducted in the same location for this risk assessment reduces some potential uncertainties since it does not involve extrapolation of the relationship across different geographic areas with different population characteristics, land uses, source mixtures and other factors.
- Adequacy of ambient NO_2 monitors as surrogate for population exposure. The Tolbert et al. (2007) study used ambient concentrations at fixed-site monitors to represent ambient exposure and for several reasons this may or may not provide a good representation of ambient NO_2 exposure for the population. The final ISA identifies the following thee components to exposure measurement error: (1) the use of average population rather than individual exposure data; (2) the difference between average personal ambient exposure and ambient concentrations at central monitoring sites; and (3) the difference between true and measured ambient concentrations (final ISA, section 1.3.2, p.1-5). While a concentration-response function may understate the effect of personal exposure to NO_2 on the incidence of a health effect, it will give

an unbiased estimate of the effect of ambient concentrations on the incidence of the health effect, if the ambient concentrations at monitoring stations provide an unbiased estimate of the ambient concentrations to which the population is exposed. If NO_2 is the causal agent, the understatement of the impact of personal exposures is not a concern, since NO_2 NAAQS are expressed in terms of ambient, not personal exposure, levels. However, if NO_2 is not the causal agent, and the effects are due to confounding copollutants or other factors, then reducing ambient NO_2 levels might not result in the estimated reductions in the health effects.

- Adjustment of air quality distributions to simulate just meeting the current annual standard and alternative 98th and 99th percentile daily maximum 1-h standards. The current annual standard and many of the alternative 1-h standards analyzed in the current risk assessment requires an upward adjustment of recent ambient NO_2 levels. In adjusting air quality to simulate just meeting these standards, we have assumed that the overall shape of the distribution of 1-h and 24-h concentrations would not change. While we believe this is a reasonable assumption in the absence of evidence supporting a change in the distribution, we recognize this as an important additional uncertainty, especially for those scenarios where considerable upward adjustment is required to simulate just meeting some of the standards.
- Baseline incidence. There are uncertainties related to the baseline incidence including: (1) the extent to which baseline incidence varies between the year used in the assessment (i.e., 2004) and some unspecified future year when air quality is adjusted to simulate just meeting the current and alternative standards; (2) the extent to which baseline incidence is underestimated because only 36 of the 42 emergency departments provided baseline incidence for the study in 2004; (3) the use of annual incidence date to develop daily baseline incidence; and (4) the extent to which Atlanta area residents visited emergency departments outside of the Atlanta MSA. As noted previously, the use of the available baseline incidence for 2004 results in some underestimation of the risk for the Atlanta MSA since data were only available from 36 of the 42 emergency departments for that year (i.e., about 14% of emergency departments were not included). Concerning the use of annual baseline incidence to estimate daily incidence, to the extent that NO_2 affects health, actual incidence would be expected to be somewhat higher than average on days with high NO_2 concentrations and using an average daily incidence would result in underestimating the changes in incidence on such days. Similarly, actual incidence would be expected to be somewhat lower on days with low NO_2 concentrations and using an average daily incidence would result in overestimating the changes in incidence on such days. Both of these effects would be expected to be small and should largely cancel each other out. With respect to the last uncertainty, we consider this to be a relatively minor uncertainty since most ED visits are likely to be made to the closest emergency department available, which, for residents of the Atlanta MSA are likely to be within that MSA. The baseline incidence data has not been adjusted for any future changes such as aging of the population over time or possible changes in ED visits due to increased in-migration of younger individuals.

9.7 RISK ESTIMATES FOR EMERGENCY DEPARTMENT VISITS

In this section, we present risk estimates associated with several air quality scenarios, including thee recent years of air quality as represented by 2005, 2006, and 2007 monitoring data. In addition, risk estimates are presented for a hypothetical scenario, where air quality from 2006 and 2007 is adjusted upward to simulate just meeting the current annual NO_2 standard, and for scenarios where the thee year period (2005-2007) is adjusted (either up or down) to simulate just meeting potential alternative 98^{th} and 99^{th} percentile daily maximum 1-h standards. As discussed previously in chapter 5, potential alternative 1-h standards with levels set at 0.05, 0.10, 0.15, and 0.20 have been included in the risk assessment.

Throughout this section and Appendix C the uncertainty surrounding risk estimates resulting from the statistical uncertainty of the NO_2 coefficients in the concentration-response functions used is characterized by ninety-five percent confidence intervals around estimates of incidence, incidence per 100,000 population, and percent of total incidence that is NO_2-related. In some cases, the lower bound of a confidence interval falls below zero. This does not imply that additional exposure to NO_2 has a beneficial effect but only that the estimated coefficient in the concentration-response function was not statistically significantly different from zero. Lack of statistical significance could reflect insufficient statistical power to detect a relationship that exists or could reflect that no relationship exists.

Tables 9-1, 9-2, and 9-3 present the risk estimates for NO_2-related ED visits associated with recent air quality (2005, 2006, and 2007, respectively). Table 9-1 for 2005 also includes risk estimates for just meeting several alternative 1-h daily maximum standards based on adjusting 2005-2007 air quality data to simulate just meeting these alternative standards. Similarly, Tables 9-2 and 9-3 include risk estimates associated with just meeting these same alternative 1-h standards, as well as risk estimates associated with a simulation where air quality is adjusted upward to represent just meeting the current 0.053 ppm annual NO_2 standard. Since attainment of the current annual standard is based on the most recent two year period, risk estimates for the annual standard are only included in the tables based on 2006 and 2007 air quality.

In Table 9-1, and similarly in Tables 9-2 and 9-3, the first row of incidence estimates is based on a single pollutant model (i.e., NO_2 only) and results in the largest estimates for NO_2-related respiratory ED visits. The next three rows present risk estimates based on two pollutant

Table 9-1. Estimated Incidence of Respiratory ED Visits Associated with "As Is" NO2 Concentrations and NO2 Concentrations that Just Meet Alternative Standards in Atlanta, GA, Based on Adjusting 2005 NO2 Concentrations.*

Other Pollutants in Model	Incidence of Respiratory Emergency Department Visits Associated with "As is" NO_2 Concentrations and NO_2 Concentrations that Just Meet Alternative Standards**								
	"as is"	Alternative 98th percentile 1-hr daily maximum standards (ppm)				Alternative 99th percentile 1-hr daily maximum standards (ppm)			
		0.05***	0.1	0.15	0.2	0.05	0.1	0.15	0.2
none	3600 (1900 - 5300)	2600 (1400 - 3800)	5100 (2700 - 7400)	7500 (4100 - 10900)	9900 (5400 - 14300)	2400 (1300 - 3500)	4700 (2500 - 6900)	7000 (3800 - 10200)	9300 (5000 - 13300)
CO	3100 (1000 - 5100)	2200 (700 - 3600)	4300 (1500 - 7200)	6400 (2200 - 10500)	8500 (2900 - 13800)	2000 (700 - 3400)	4000 (1400 - 6700)	6000 (2000 - 9800)	7900 (2700 - 12900)
O_3	1800 (-100 - 3700)	1300 (-100 - 2600)	2600 (-100 - 5200)	3900 (-200 - 7700)	5100 (-200 - 10200)	1200 (-100 - 2500)	2400 (-100 - 4900)	3600 (-200 - 7200)	4800 (-200 - 9500)
PM_{10}	1300 (-700 - 3300)	900 (-500 - 2300)	1800 (-1000 - 4600)	2700 (-1600 - 6800)	3600 (-2100 - 9000)	800 (-500 - 2200)	1700 (-1000 - 4300)	2500 (-1500 - 6400)	3400 (-1900 - 8400)
PM_{10}, O_3	700 (-1400 - 2800)	500 (-1000 - 2000)	1000 (-2000 - 4000)	1600 (-3000 - 5900)	2100 (-4000 - 7800)	500 (-900 - 1900)	1000 (-1800 - 3700)	1500 (-2800 - 5500)	1900 (-3700 - 7300)

*Estimated incidences of respiratory emergency department visits are based on the concentration-response functions estimated in Tolbert et al. (2007) [results corresponding to Figure 2 in Tolbert et al. (2007) were obtained via personal communication with P. Tolbert]. All models use a 3-day moving average of the daily 1-hr. maximum NO_2 concentration and apply to all ages.

**Incidence was quantified down to 0 ppb. Incidences are rounded to the nearest 100.

***Alternative 1-hr daily maximum standards are characterized by a concentration of m ppm and an nth percentile, requiring that the average of the 3 annual nth percentile 1-hr daily maxima over a 3-year period be at or below m ppm.

Note: Numbers in parentheses are 95% confidence intervals based on statistical uncertainty surrounding the NO_2 coefficient.

Table 9-2. Estimated Incidence of Respiratory ED Visits Associated with "As Is" NO2 Concentrations and NO2 Concentrations that Just Meet Alternative Standards in Atlanta, GA, Based on Adjusting 2006 NO2 Concentrations.*

Other Pollutants in Model	Incidence of Respiratory Emergency Department Visits Associated with "As is" NO_2 Concentrations and NO_2 Concentrations that Just Meet the Current and Alternative Standards**									
	"as is"	current annual standard	Alternative 98th percentile 1-hr daily maximum standards (ppm)				Alternative 99th percentile 1-hr daily maximum standards (ppm)			
			0.05***	0.1	0.15	0.2	0.05	0.1	0.15	0.2
none	3800 (2000 - 5500)	10900 (5900 - 15700)	2700 (1400 - 3900)	5300 (2800 - 7700)	7800 (4200 - 11300)	10300 (5600 - 14800)	2500 (1300 - 3600)	4900 (2600 - 7200)	7300 (3900 - 10600)	9600 (5200 - 13900)
CO	3200 (1100 - 5300)	9400 (3200 - 15200)	2300 (800 - 3800)	4500 (1500 - 7400)	6700 (2300 - 11000)	8800 (3000 - 14400)	2100 (700 - 3500)	4200 (1400 - 6900)	6200 (2100 - 10200)	8200 (2800 - 13400)
O_3	1900 (-100 - 3900)	5600 (-300 - 11200)	1400 (-100 - 2700)	2700 (-100 - 5400)	4000 (-200 - 8000)	5300 (-200 - 10600)	1300 (-100 - 2600)	2500 (-100 - 5100)	3700 (-200 - 7500)	4900 (-200 - 9900)
PM_{10}	1300 (-800 - 3400)	4000 (-2300 - 9900)	900 (-500 - 2400)	1900 (-1100 - 4800)	2800 (-1600 - 7100)	3700 (-2200 - 9400)	900 (-500 - 2300)	1800 (-1000 - 4500)	2600 (-1500 - 6600)	3500 (-2000 - 8700)
PM_{10}, O_3	800 (-1500 - 2900)	2300 (-4400 - 8600)	500 (-1000 - 2100)	1100 (-2100 - 4100)	1600 (-3100 - 6200)	2200 (-4200 - 8100)	500 (-1000 - 1900)	1000 (-1900 - 3900)	1500 (-2900 - 5700)	2000 (-3900 - 7600)

*Estimated incidences of respiratory emergency department visits are based on the concentration-response functions estimated in Tolbert et al. (2007) [results corresponding to Figure 2 in Tolbert et al. (2007) were obtained via personal communication with P. Tolbert]. All models use a 3-day moving average of the daily 1-hr. maximum NO_2 concentration and apply to all ages.

**Incidence was quantified down to 0 ppb. Incidences are rounded to the nearest 100.

***Alternative 1-hr daily maximum standards are characterized by a concentration of m ppm and an nth percentile, requiring that the average of the 3 annual nth percentile 1-hr daily maxima over a 3-year period be at or below m ppm.

Note: Numbers in parentheses are 95% confidence intervals based on statistical uncertainty surrounding the NO_2 coefficient.

Table 9-3. Estimated Incidence of Respiratory ED Visits Associated with "As Is" NO_2 Concentrations and NO_2 Concentrations that Just Meet Alternative Standards in Atlanta, GA, Based on Adjusting 2007 NO_2 Concentrations.*

Other Pollutants in Model	Incidence of Respiratory Emergency Department Visits Associated with "As is" NO_2 Concentrations and NO_2 Concentrations that Just Meet the Current and Alternative Standards**									
	"as is"	current annual standard	Alternative 98th percentile 1-hr daily maximum standards (ppm)				Alternative 99th percentile 1-hr daily maximum standards (ppm)			
			0.05***	0.1	0.15	0.2	0.05	0.1	0.15	0.2
none	3400 (1800 - 4900)	9800 (5300 - 14200)	2400 (1300 - 3500)	4700 (2500 - 6900)	7000 (3800 - 10200)	9300 (5000 - 13400)	2200 (1200 - 3300)	4400 (2400 - 6400)	6500 (3500 - 9500)	8600 (4700 - 12500)
CO	2900 (1000 - 4800)	8400 (2900 - 13700)	2000 (700 - 3400)	4000 (1300 - 6700)	6000 (2000 - 9900)	7900 (2700 - 12900)	1900 (600 - 3200)	3800 (1300 - 6200)	5600 (1900 - 9200)	7400 (2500 - 12100)
O_3	1700 (-100 - 3500)	5100 (-200 - 10100)	1200 (-100 - 2500)	2400 (-100 - 4900)	3600 (-200 - 7200)	4800 (-200 - 9500)	1100 (-100 - 2300)	2200 (-100 - 4500)	3300 (-200 - 6700)	4400 (-200 - 8900)
PM_{10}	1200 (-700 - 3000)	3600 (-2100 - 8900)	800 (-500 - 2200)	1700 (-1000 - 4300)	2500 (-1500 - 6400)	3400 (-1900 - 8400)	800 (-400 - 2000)	1600 (-900 - 4000)	2400 (-1400 - 5900)	3100 (-1800 - 7800)
PM_{10}, O_3	700 (-1300 - 2600)	2100 (-4000 - 7800)	500 (-900 - 1900)	1000 (-1800 - 3700)	1500 (-2800 - 5500)	1900 (-3700 - 7300)	500 (-900 - 1700)	900 (-1700 - 3500)	1400 (-2600 - 5100)	1800 (-3400 - 6800)

*Estimated incidences of respiratory emergency department visits are based on the concentration-response functions estimated in Tolbert et al. (2007) [results corresponding to Figure 2 in Tolbert et al. (2007) were obtained via personal communication with P. Tolbert]. All models use a 3-day moving average of the daily 1-hr. maximum NO_2 concentration and apply to all ages.

**Incidence was quantified down to 0 ppb. Incidences are rounded to the nearest 100.

***Alternative 1-hr daily maximum standards are characterized by a concentration of m ppm and an nth percentile, requiring that the average of the 3 annual nth percentile 1-hr daily maxima over a 3-year period be at or below m ppm.

Note: Numbers in parentheses are 95% confidence intervals based on statistical uncertainty surrounding the NO_2 coefficient.

models (i.e., NO_2 + CO, NO_2 + O_3, NO_2 + PM_{10}). The last row presents risk estimates based on a three pollutant model (i.e., NO_2 + PM_{10} + O_3). As noted above in this chapter, effect estimates based on a multi-pollutant model can be uncertain and even result in statistically insignificant estimates where there is a true relationship, if the co-pollutants included in the model are highly correlated with NO_2. The negative lower bounds of the confidence intervals for many of the risk estimates based on multi-pollutant models is the result of this problem and staff do not view this as suggesting any health beneficial effect of increasing NO_2 exposure levels.

Tables 4-4, 4-5, and 4-6 in Appendix C present these same risk estimates expressed in terms of incidence per 100,000 general population in the Atlanta MSA based on recent air quality and simulating just meeting alternative standards based on 2005, 2006, an 2007 air quality data. Finally, Tables 4-7, 4-8, and 4-9 in Appendix C present these same risk estimates in terms of percent of total incidence of ED visits for the Atlanta MSA based on the same three years of air quality data.

Key Observations

Presented below are key observations resulting from the respiratory-related ED visits risk assessment:

- Respiratory-related ED visits estimated to result from exposures to NO_2 were estimated for a single urban area (i.e., Atlanta) for several recent years of air quality (2005-2007) and for air quality adjusted to simulate just meeting the current annual NO_2 standard and several alternative 1-hour daily maximum NO_2 standards. While we would expect some differences in estimated NO_2-related ED respiratory visits across different locations due to differences in populations, land use patterns, access to medical facilities, co-pollutants and other factors affecting exposure and the concentration-response relationships, we believe that the risk estimates do provide a useful perspective on the likely overall magnitude and pattern of ED visits associated with various NO_2 air quality scenarios in urban areas within the U.S.
- The largest risk estimates were associated with single-pollutant NO_2 concentration-response functions based on the effect estimates reported in Tolbert et al. (2007). Risk estimates based on various co-pollutant models with O_3, CO, and PM_{10} resulted in significant reduction in the risk estimates, often by a factor of two or greater and resulted in much wider confidence intervals.
- The only standards that resulted in a reduction in risk estimates from the baseline of recent air quality for the three year period examined were the 98^{th} and 99^{th} percentile 1-hour daily maximum standards set at the level of 0.05 ppm.
- The impact of changing the level of the alternative 1-hour daily maximum standards is substantially greater than the impact of changing from a 98th to a

99th percentile standard. For example, changing from a 98th percentile 1-hour daily maximum standard based on 0.05 ppm to one based on 0.1 ppm reduces the estimated incidence of respiratory-related ED visits in Atlanta by about 49 percent in 2007 (from 4700 to 2400); however, changing from a 98th percentile 1-hour daily maximum standard based on 0.05 ppm to a 99th percentile 1-hour daily maximum standard based on 0.05 reduces the incidence in 2007 by only about 8 percent (from 2400 to 2200).

- The overall pattern of risk estimates is similar across the three years examined. For the three years examined, there was not significant year-to-year variability in the risk estimates.
- Important uncertainties and limitations associated with the risk assessment which were discussed above in section 9.6 and which should be kept in mind as one considers the quantitative risk estimates include:
  - uncertainty about the extent to which the associations between NO_2 and ED visits for respiratory causes actually reflect causal relationships;
  - statistical uncertainty due to sampling error which is characterized in the assessment;
  - uncertainties associated with the air quality adjustment procedure that was used to simulate just meeting the current annual and several alternative 1-h daily maximum standards;
  - uncertainties associated with the estimated baseline incidence for ED respiratory visits;
  - uncertainties related to how changes in population, activity patterns, air quality, and other factors over time might impact the risk estimates;
  - there is uncertainty about the extent to which the risk estimates presented for the Atlanta urban area are representative of other urban locations in the U.S..

10. References

AHS. (2003a). American Housing Survey for 2003. Available at: http://www.census.gov/hhes/www/housing/ahs/ahs.html.

AHS. (2003b). Source and Accuracy Statement for the 2003 AHS-N Data Chart. Available at: http://www.census.gov/hhes/www/housing/ahs/03dtchrt/source.html

Barck, C, Sandström T, Lundahl J, Halldén G, Svartengren M, Strand V, Rak S, Bylin G. (2002). Ambient level of NO_2 augments the inflammatory response to inhaled allergen in asthmatics. *Respir Med*. 96:907-917.

Barck, C, Lundahl J, Halldén G, Bylin G. (2005). Brief exposures to NO_2 augment the allergic inflammation in asthmatics. *Environ Res*. 97:58-66.

Beckerman, B, Jerrett M, Brook JR, Verma DK, Arain MA, Finkelstein MM. (2008). Correlation of nitrogen dioxide with other traffic pollutants near a major expressway. *Atmos Environ*. 42:275-290.

Bell, S and Ashenden TW. (1997). Spatial and temporal variation in nitrogen dioxide pollution adjacent to rural roads. *Water Air Soil Pollut*. 95:87-98.

Brauer, M, Hoek G, Smit HA, De Jongste JC, Gerritsen J, Postma DS, Kerkhof M, Brunekreef B. (2007). Air pollution and development of asthma, allergy and infections in a birth cohort. *Eur. Respir. J*. 29:879-888.

Bylin, G, Lindvall T, Rehn T, Sundin B. (1985) Effects of short-term exposure to ambient nitrogen dioxide concentrations on human bronchial reactivity and lung function. *Eur. J. Respir. Dis*. 66:205-217.

Cape, JN, Tang YS, van Dijk N, Love L, Sutton MA, Palmer SCF. (2004). Concentrations of ammonia and nitrogen dioxide at roadside verges, and their contribution to nitrogen deposition. *Environ Pollut*. 132:469-478.

CARB. (2001). Indoor air quality: residential cooking exposures. Final report. California Air Resources Board, Sacramento, California. Available at: http://www.arb.ca.gov/research/indoor/cooking/cooking.htm.

Chan, AT and Chung MW. (2003). Indoor-outdoor air quality relationships in vehicle: effect of driving environment and ventilation modes. *Atmos Environ*. 37:3795-3808.

Chauhan, AJ, Inskip HM, Linaker CH, Smith S, Schreiber J, Johnston SL, Holgate ST (2003). Personal exposure to nitrogen dioxide (NO2) and the severity of virus-induced asthma in children. *Lancet* 361:1939-1944.

Clougherty, JE, Levy JI, Kubzansky LD, Ryan PB, Suglia SF, Canner MJ, and Wright RJ. (2007). Synergistic effects of traffic-related air pollution and exposure to violence on urban asthma etiology. *Environ. Health Perspect.* 115:1140-1146.

Delfino, RJ, Gone H, Linn WS, Pellizzari ED, Hu Y. (2003). Asthma symptoms in Hispanic children and daily ambient exposures to toxic and criteria air pollutants. *Environ. Health Perspect.* 111:647-656.

Delfino, RJ, Zeiger RS, Seltzer JM, Street DH, McLaren CE. (2002). Association of asthma symptoms with peak particulate air pollution and effect modification by anti-inflammatory medication use. *Environ. Health Perspect.* 110:A607-A617.

Devalia, JL, Rusznak C, Herdman MJ, Trigg CJ, Tarraf H, Davies RJ. (1994) Effect of nitrogen dioxide and sulphur dioxide on airway response of mild asthmatic patients to allergen inhalation. *Lancet* 344:1668-1671.

Dietert, RR, Etzel RA, Chen D, Halonen M, Holladay SD, Jarabek AM, Landreth K, Peden DB, Pinkerton K, Smialowicz RJ, Zoetis T. (2000). Workshop to identify critical window of exposure for children's health: immune and respiratory systems work group summary. *Environ Health Perspect*. Suppl. 108(3):483-490.

EPA. (1982). Air Quality Criteria for Oxides of Nitrogen. National Center for Environmental Assessment, Research Triangle Park, NC. EPA-600/8-82-026. Available at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=44436.

EPA. (1993). Air Quality Criteria Document for the Oxides of Nitrogen. National Center for Environmental Assessment, Research Triangle Park, NC. EPA-600/8-91/049F. Available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=40179.

EPA. (1995). Review of the National Ambient Air Quality Standards for Nitrogen Dioxide: Assessment of Scientific and Technical Information. OAQPS Staff Paper. Office of Air Quality Planning and Standards, Research Triangle Park, NC. EPA-452/R-95-005. September 1995.

EPA. (2002). Consolidated Human Activities Database (CHAD) Users Guide. Database and documentation available at: http://www.epa.gov/chadnet1/.

EPA. (2004). AERMOD: Description of Model Formulation. Office of Air Quality Planning and Standards, Research Triangle Park, NC. EPA-454/R-03-004. Available at: http://www.epa.gov/scram001/7thconf/aermod/aermod_mfd.pdf.

EPA. (2006a). Total Risk Integrated Methodology (TRIM) - Air Pollutants Exposure Model Documentation (TRIM.Expo / APEX, Version 4) Volume I: User's Guide. Office of Air Quality Planning and Standards, Research Triangle Park, NC. June 2006. Available at: http://www.epa.gov/ttn/fera/human_apex.html.

EPA. (2006b). Total Risk Integrated Methodology (TRIM) - Air Pollutants Exposure Model Documentation (TRIM.Expo / APEX, Version 4) Volume II: Technical Support Document. Office of Air Quality Planning and Standards, Research Triangle Park, NC. Available at: http://www.epa.gov/ttn/fera/human_apex.html.

EPA. (2007a). Plan for Review of the Primary National Ambient Air Quality Standard for Nitrogen Dioxide. Available at: http://www.epa.gov/ttn/naaqs/standards/nox/s_nox_cr_pd.html.

EPA. (2007b). Nitrogen Dioxide Health Assessment Plan: Scope and Methods for Exposure and Risk Assessment. Office of Air Quality Planning and Standards, Research Triangle Park, NC. Available at: http://www.epa.gov/ttn/naaqs/standards/nox/s_nox_cr_pd.html.

EPA. (2007c). US EPA Air Quality System (AQS). Download Detailed AQS Data. Available at: http://www.epa.gov/ttn/airs/airsaqs/detaildata/downloadaqsdata.htm.

EPA (2007d). Field Guide to Air Quality Data (v1.0.0). February 28, 2007. Available at: http://www.epa.gov/ttn/airs/aqsdatamart/documentation/index.htm.

EPA. (2007e). 2002 National Emissions Inventory Data & Documentation. Office of Air Quality Planning and Standards, Research Triangle Park, NC. Available at: http://www.epa.gov/ttn/chief/net/2002inventory.html.

EPA. (2007f). Clean Air Markets - Data and Maps. Office of Atmospheric Programs, Washington, DC. Emissions Prepackaged Data Sets. Available at: http://camddataandmaps.epa.gov/gdm/index.cfm?fuseaction=emissions.wizard.

EPA. (2007g). Ozone Population Exposure Analysis for Selected Urban Areas (July 2007). Office of Air Quality Planning and Standards, Research Triangle Park, NC. EPA-452/R-07-010. Available at: http://epa.gov/ttn/naaqs/standards/ozone/s_o3_cr_td.html.

EPA. (2007h). Review of the National Ambient Air Quality Standards for Ozone: Assessment of Scientific and Technical Information. OAQPS Staff paper. Office of Air Quality

Planning and Standards, Research Triangle Park, NC. EPA-452/R-07-007a. Available at: http://epa.gov/ttn/naaqs/standards/ozone/s_o3_cr_sp.html.

EPA. (2008a). ISA for Oxides of Nitrogen - Health Criteria. National Center for Environmental Assessment, Research Triangle Park, NC. Available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=194645.

EPA (2008b). Risk and Exposure Assessment to Support the Review of the NO_2 Primary National Ambient Air Quality Standard: First Draft. Office of Air Quality Planning and Standards, Research Triangle Park, NC.

Finlayson-Pitts, BJ and Pitts JN. (2000). Chemistry of the Upper and Lower Atmosphere. Academic Press, San Diego CA. Page 17.

Folinsbee, LJ. (1992). Does nitrogen dioxide exposure increase airways responsiveness? *Toxicol Ind Health*. 8:273-283.

Gauderman, W J, Avol E, Gilliland F, Vora H, Thomas D, Berhane K, McConnell R, Kuenzli N, Lurmann F, Rappaport E, Margolis H, Bates D, Peters J. (2004). The effect of air pollution on lung development from 10 to 18 years of age. *N. Engl. J. Med.* 351:1057-1067.

Gauderman, WJ, Avol E, Lurmann F, Kuenzli N, Gilliland F, Peters J, McConnell R. (2005). Childhood asthma and exposure to traffic and nitrogen dioxide. *Epidemiology* 16:737-743.

Ghenu, A, Rosant J-M, Sini J-F. (2007). Dispersion of pollutants and estimation of emissions in a street canyon in Rouen, France. *Environmental Modeling & Software*. 23:314-321.

Gilbert, NL, Woodhouse S, Stieb DM, Brook JR. (2003). Ambient nitrogen dioxide and distance from a major highway. *Sci Total Environ*. 312:43-46.

Graham, SE and McCurdy T. (2004). Developing meaningful cohorts for human exposure models. *J Expos Anal Environ Epidemiol*. 14(1)23-43.

Heeb, NV, Saxer CJ, Forss AM, Bruhlmann S. (2008). Trends of NO-, NO_2-, and NH_3-emissions from gasoline-fueled Euro-3- to Euro-4-passenger cars. *Atmos Environ*. 42:2543-2554

Ito, K. (2007). Association between doarse particles and asthma emergency department (ED) visits in New York City. Presented at: American Thoracic Society international conference; San Francisco, CA.

Jaffe, DH, Singer ME, Rimm AA. (2003). Air pollution and emergency department visits for asthma among Ohio Medicaid recipients, 1991-1996. *Environ. Res.* 91:21-28.

Jenkins, HS, Devalia JL, Mister RL, Bevan AM, Rusznak C, Davies RJ. (1999). The effect of exposure to ozone and nitrogen dioxide on the airway response of atopic asthmatics to inhaled allergen: dose- and time-dependent effects. *Am. J. Respir. Crit. Care Med.* 160:33-39.

Johnson, T, Mihlan G, LaPointe J, Fletcher K, Capel J. (1999). Estimation Of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels In Denver Residents Using pNEM/CO (version 2.0). Prepared by ICF Kaiser Consulting Group for the U.S. Environmental Protection Agency under Contract No. 68-D6-0064, March 1999.

Jörres, R, Magnussen H. (1990). Airways response of asthmatics after a 30 min exposure, at resting ventilation, to 0.25 ppm NO_2 or 0.5 ppm SO_2. *Eur. Respir. J.* 3:132-137.

Jörres, R, Magnussen H. (1991). Effect of 0.25 ppm nitrogen dioxide on the airway response to methacholine in asymptomatic asthmatic patients. *Lung* 169:77-85.

Jörres, R, Nowak D, Grimminger F, Seeger W, Oldigs M, Magnussen H. (1995). The effect of 1 ppm nitrogen dioxide on bronchoalveolar lavage cells and inflammatory mediators in normal and asthmatic subjects. *Eur Respir J.* 8:416-424.

Kim, S-Y, O'Neill M, Lee J-T, Cho Y, Kim J, and Kim H. (2007). Air pollution, socioeconomic position, and emergency hospital visits for asthma in Seoul, Korea. *Int. Arch. Occup. Environ. Health* 80:701-710.

Koontz, MD, Mehegan LL, and Nagda NL. (1992). Distribution and Use of Cooking Appliances That Can Affect Indoor Air Quality, Report No. GRI-93/0013. Gas Research Institute, Chicago, IL.

Langstaff, JE. (2007). OAQPS Staff Memorandum to Ozone NAAQS Review Docket (OAR-2005-0172). Subject: Analysis of Uncertainty in Ozone Population Exposure Modeling. [January 31, 2007]. Available at: http://www.epa.gov/ttn/naaqs/standards/ozone/s_o3_cr_td.html.

Linn, WS, Shamoo DA, Anderson KR, Peng RC, Avol EL, Hackney JD, Gong, H Jr. (1996). Short-term air pollution exposures and responses in Los Angeles area schoolchildren. *J. Exposure Anal. Environ. Epidemiol.* 6:449-472.

Linn, WS, Szlachcic Y, Gong H, Kinney PL, Berhane KT. (2000). Air pollution and daily hospital admissions in metropolitan Los Angeles. *Environ. Health Perspect.* 108:427-434.

McCurdy, TR. (1994). Analysis of high 1 hour NO_2 values and associated annual averages using 1988-1992 data. Office of Air Quality Planning and Standards, Research Triangle Park, NC. Available in Docket A-93-06.

McCurdy, T, Glen G, Smith L, Lakkadi Y. (2000). The National Exposure Research Laboratory's Consolidated Human Activity Database. *J Exp Anal Environ Epidemiol*. 10: 566-578.

McCurdy T and Graham SE. (2003). Using human activity data in exposure models: analysis of discriminating factors. *J Expos Anal Environ Epidemiol*. 13:294-317.

Mohsenin, V. (1987) Airway responses to nitrogen dioxide in asthmatic subjects. *J. Toxicol. Environ. Health* 22:371-380.

Mortimer, KM, Neas LM, Dockery DW, Redline S, Tager IB. (2002). The effect of air pollution on inner-city children with asthma. *Eur Respir J*. 19:699-705.

National Cooperative Highway Research Program (NCHRP) (1997). Recommended Procedure for Long-Range Transportation Planning and Sketch Planning, NCHRP Report 387, National Academy Press. 151 pp., ISBN No: 0-309-060-58-3.

National Heart, Lung, and Blood Institute (NHLBI). (2007) Expert panel report 3: guidelines for the diagnosis and management of asthma. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Asthma Education and Prevention Program; NIH Publication No. 07-4051.

New York Department of Health. (2006). A study of ambient air contaminants and asthma in New York City, Final Report Part B: Air contaminants and emergency department visits for asthma in the Bronx and Manhattan. Prepared for: The U.S. Department of Health and Human Services, Agency for Toxic Substance and Disease Registry.

Oftedal, B, Brunekreef B, Nystad W, Madsen C, Walker SE, Nafstad P. (2008). Residential outdoor air pollution and lung function in schoolchildren. *Epidemiology* 19:129-137.

Ostro, B, Lipsett M, Mann J, Braxton-Owens H, White M. (2001). Air pollution and exacerbation of asthma in African-American children in Los Angeles. *Epidemiology* 12:200-208.

Peel, JL, Tolbert PE, Klein M, Metzger KB, Flanders WD, Knox T, Mulholland JA, Ryan PB, Frumkin H. (2005). Ambient air pollution and respiratory emergency department visits. *Epidemiology*. 16:164-174.

Persily, A, Gorfain J, Brunner G. (2005). Ventilation design and performance in U.S. office buildings. *ASHRAE Journal*. April 2005, 30-35.

Pilotto, LS, Douglas RM, Attewell RG, Wilson SR (1997) Respiratory effects associated with indoor nitrogen dioxide exposure in children. Int. J. Epidemiol. 26: 788-796.

Pilotto, LS, Nitschke M, Smith BJ, Pisaniello D, Ruffin RE, McElroy HJ, Martin J, Hiller JE. (2004). Randomized controlled trial of unflued gas heater replacement on respiratory health of asthmatic schoolchildren. *Int J Epidemiol*. 33:208-214.

Pleijel, H, Karlsson GP, Gerdin EB. (2004). On the logarithmic relationship between NO_2 concentration and the distance from a highroad. *Sci Total Environ*. 332:261-264.

Rodes, C, Sheldon L, Whitaker D, Clayton A, Fitzgerald K, Flanagan J, DiGenova F, Hering S, Frazier C. (1998). Measuring Concentrations of Selected Air Pollutants Inside California Vehicles. California Environmental Protection Agency, Air Resources Board. Final Report, December 1998.

Rodes, CE and Holland DM. (1981). Variations of NO, NO_2 and O_3 concentrations downwind of a Los Angeles freeway. *Atmos Environ*. 15:243-250.

Roger, LJ, Horstman DH, McDonnell W, Kehrl H, Ives PJ, Seal E, Chapman R, Massaro E. (1990). Pulmonary function, airway responsiveness, and respiratory symptoms in asthmatics following exercise in NO_2. *Toxicol. Ind. Health* 6:155-171.

Romieu, I, Ramírez-Aguilar M., Sienra-Monge JJ, Moreno-Macías, H, Del Rio-Navarro BE, David G, Marzec J, Hernández-Avila M, London S. (2006). GSTM1 and GSTP1 and respiratory health in asthmatic children exposed to ozone. *Eur. Respir. J.* 28:953-959.

Rojas-Martinez, R, Perez-Padilla R, Olaiz-Fernandez G, Mendoza-Alvarado L, Moreno-Macias H, Fortoul T, McDonnell W, Loomis D, Romieu I. (2007a) Lung function growth in children with long-term exposure to air pollutants in Mexico City. *Am. J. Respir. Crit. Care Med.* 176:377-384.

Rojas-Martinez, R, Perez-Padilla R, Olaiz-Fernandez G, Mendoza-Alvarado L, Moreno-Macias H, Fortoul T, McDonnell W, Loomis D, Romieu I. (2007b) Lung function growth in children with long-term exposure to air pollutants in Mexico City. Online data supplement. Available: http://ajrccm.atsjournals.org/cgi/data/176/4/377/DC1/1 [3 October, 2007].

Roorda-Knape, MC, Janssen NAH, De Hartog JJ, Van Vliet PHN, Harssema H, Brunekreef B. (1998). Air Pollution from traffic in city districts near major roadways. *Atmos Environ*. 32(11)1921-1930.

Rubenstein, I, Bigby BG, Reiss TF, Boushey HA Jr. (1990) Short-term exposure to 0.3 ppm nitrogen dioxide does not potentiate airway responsiveness to sulfur dioxide in asthmatic subjects. *Am. Rev. Respir. Dis.* 141:381-385.

Schildcrout, JS, Sheppard L, Lumley T, Slaughter JC, Koenig JQ, Shapiro GG. (2006). Ambient air pollution and asthma exacerbations in children: an eight-city analysis. *Am J Epidemiol*. 164:505-517.

Schwartz, J, Dockery DW, Neas LM, Wypij D, Ware JH, Spengler JD, Koutrakis P, Speizer FE, Ferris BG, Jr. (1994). Acute effects of summer air pollution on respiratory symptom reporting in children. *Am J Respir Crit Care Med*. 150:1234-1242.

Shorter, JH, Herndon S, Zahniser MS, Nelson DD, Wormhoudt J, Demerjian KL, Kolb CE. (2005). Real-Time Measurements of Nitrogen Oxide Emissions from In-Use New York City Transit Buses Using a Chase Vehicle. *Environ Sci Technol.* 39:7991-8000.

Spicer, CW, Kenny DV, Ward GF, Billick IH. (1993). Transformations, lifetimes, and sources of NO_2, HONO, and HNO_3 in indoor environments. *JAWMA*. 43(11):1479-1485.

Strand, V, Salomonsson P, Lundahl J, Bylin G. (1996). Immediate and delayed effects of nitrogen dioxide exposure at an ambient level on bronchial responsiveness to histamine in subjects with asthma. *Eur Respir J*. 9:733-740.

Strand, V, Rak S, Svartengren M, Bylin G. (1997). Nitrogen dioxide exposure enhances asthmatic reaction to inhaled allergen in subjects with asthma. *Am J Respir Crit Care Med*. 155:881-887.

Strand, V, Svartengren M, Rak S, Barck C, Bylin G. (1998). Repeated exposure to an ambient level of NO_2 enhances asthmatic response to nonsymptomatic allergen dose. *Eur Respir J*. 12:6-12.

Tolbert, PE, Klein M, Peel JL, Sarnat SE, Sarnat JA. (2007). Multipollutant modeling issues in a study of ambient air quality and emergency department visits in Atlanta. *J Expos Sci Environ Epidemiol*. 17S2:S29-35.

Tunnicliffe, WS, Burge PS, Ayres JG. (1994) Effect of domestic concentrations of nitrogen dioxide on airway responses to inhaled allergen in asthmatic patients. *Lancet* 344:1733-1736.

US DOT. (2007). Part 3-The Journey To Work files. Bureau of Transportation Statistics (BTS). Available at: http://transtats.bts.gov/.

Vardoulakis, S, Gonzalez-Flesca N, Fisher BEA, Pericleous K. (2004). Spatial variability of air pollution in the vicinity of a permanent monitoring station in central Paris. *Atmos. Environ.* 39:2725-2736.

Westerdahl, D, Fruin S, Sax T, Fine PM, Sioutas C. (2005). Mobile platform measurements of ultrafine particles and associated pollutant concentrations on freeways and residential streets in Los Angeles. *Atmos Environ*. 39:3597-3610.

Witten, A, Solomon C, Abbritti E, Arjomandi M, Zhai W, Kleinman M, Balmes J. (2005). Effects of nitrogen dioxide on allergic airway responses in subjects with asthma. *J. Occup. Environ. Med.* 47:1250-1259.

Wolff, GT. (1993). Letter to EPA Administrator Carol Browner: "CASAC Closure on the Air Quality Criteria Document for Oxides of Nitrogen." EPA-SAB-CASAC-LTR-93-015, September 30.

Wolff, GT. (1995). Letter to EPA Administrator Carol Browner: "CASAC Review of the Staff Paper for the Review of the National Ambient Air Quality Standards for Nitrogen Dioxide: Assessment of Scientific and Technical Information." EPA-SAB-CASAC-LTR-95-004, August 22.

Yao, X, Lau NT, Chan CK, Fang M. (2005). The use of tunnel concentration profile data to determine the ratio of NO_2/NO_x directly emitted from vehicles. *Atmos Chem Phys Discuss*. 5:12723–12740. Available at: http://www.atmos-chem-phys-discuss.net/5/12723/2005/acpd-5-12723-2005.pdf.

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